SEPARATION OF ^{103}Pd FROM Ag AND Rh TARGETS FOR PRODUCTION OF '^{103}Pd SEEDS' FOR PROSTATE CANCER BRACHYTHERAPY

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Declaration

I, the undersigned, declare that the work contained in this dissertation is my own original work and has not previously in its entirely or in part been submitted at any university for a degree.

Singature: **Date:**

SUMMARY

Radiochemical separation of ^{103}Pd from ^{nat}Ag, using a 66 MeV proton-induced reaction at iThemba LABS, was studied and a radiochemical method was developed for the separation. For the separation, which comprises the separation of Pd from a large amount of target material (16 g Ag), as well as Rh radioisotopes produced from decay of their Pd parents (mainly ^{101}Rh and ^{100}Rh), three ion exchange resins were tested: a Chelex 100 chelating resin, the AG 1-X8 anion exchange resin and a AG MP-1 anion exchange resin. For the optimum elution of Pd from the latter two resins, two elution curves using water and 5% ammonia solution, were obtained. With an average recovery of 97.4% and sharper elution curve from the macroporous AG MP-1, this resin was finally chosen for routine production. To achieve the separation, a simple, easily operated radiochemical processing system was designed and installed in a hot cell.

Radiochemical separation of ^{103}Pd from a Rh target was also studied and several cation and anion exchange resins were tested. A carrier-free separation of ^{103}Pd was developed, using an AG 1-X8 anion exchange resin. Bombarded tablets of $RhCl_3.3H_2O$, as the targets, were used for these separations. The procedure, originally designed for the separation of Pd from Cu and Rh, was modified using H_2O_2 for the oxidation of Ru prior to the sorption on the resin and successfully used for the separation of isotopes of Rh from the isotopes of Pd, Ru, Tc, Nb, Mo, Zr and Y, which were produced by 400 MeV ^{16}O- and ^{12}C-induced $RhCl_3.3H_2O$ targets. To elute the Pd from the resin, 5% ammonia solution was used; the recovery was about 92%.

To prepare the Rh target for routine production, an electroplating method of Rh on a Cu substrate was developed. $Rh(ClO_4)_3$, in 0.5 M perchloric acid, was used as the electrolyte bath. The electroplated Rh was then dissolved by an alternating current technique, using 6 M HCl and a current density of 2 A/cm^2.

For production of the seeds, ^{103}Pd was sorbed on the weakly basic anion exchange resin Amberlite IRA-93 (600-700 μ), by recycling a 0.5 M HCl solution of Pd through a 0.5 cm × 1 cm column for 2 hours. The distribution of ^{103}Pd on the resin beads was measured and RSD of 5.7% was obtained.

A funnel was designed to transfer the ^{103}Pd-loaded resin beads into the Ti tubes to prepare the seeds (0.7 mm I.D., 0.8 mm O.D., and 4.5 mm length). To enclose the tubes as capsules, the end caps were made from 0.02 mm Ti sheet and several pieces were designed and machined for the welding of the caps to the tubes. A spot-welding machine was used for the welding, after small, but vital modifications.

OPSOMMING

Palladium-103 kan volgens twee produksieroetes by iThemba LABS vervaardig word, naamlik deur die volgende protongeïnduseerde reaksies:

$^{nat}Ag(p,xn)^{103}Cd$ ($t_{½}$ =7.3 m) → ^{103}Ag ($t_{½}$ =1.1 h) → ^{103}Pd en

$^{103}Rh(p,n) \rightarrow {}^{103}Pd$.

'n Radiochemiese metode om ^{103}Pd van die Ag-skyfmateriaal te skei, is ontwikkel. Hierdie metode, wat gebaseer is op anioonuitruilerchromatografie met die makroporeuse hars AG MP-1, behels die skeiding van ^{103}Pd van 'n groot hoeveelheid skyfmateriaal (16g Ag), sowel as van Rh-radionukliede (hoofsaaklik ^{100}Rh en ^{101}Rh), wat geproduseer word deur die verval van hulle Pd-moederisotope. As die Pd met 5% ammonia oplossing geëlueer word, is 'n 97.4% herwinning moontlik. 'n Radiochemiese paneel is ontwerp, gebou en in 'n warmsel geïnstalleer vir roetine produksie.

'n Metode om Rh op 'n kopersubstraat te elektroplateer is ook ontwikkel om 'n Rh-skyf te verkry vir die protonbombardement. 'n Oplossing van 0.5 M $HClO_4$ - $Rh(HClO_4)_3$ is as die elektrolietbad gebruik. Die geëlektroplateerde Rh is opgelos in 6 M HCl deur gebruik te maak van 'n wisselstroomtegniek, met 'n stroomdigtheid van 2A/cm^2. 'n Metode om "draervrye" ^{103}Pd vanaf die Rh-skyfmateriaal te skei, is ook ontwikkel.

Gebombardeerde pille van $RhCl_3.3H_2O$ is as skywe gebruik in die onaktiewe studies. AG1-X8 anioonuitruilerhars is vir hierdie skeidings gebruik en daar is gebruik gemaak van 'n metode wat oorspronklik ontwerp is vir die skeiding van Pd van Cu en Rh. Hierdie prosedure is net effens aangepas deur H_2O_2 te gebruik vir die oksidasie van Ru, alvorens dit op die hars gesorbeer is. Hierdie metode is ook suksesvol gebruik vir die isolering van Rh van radionukliede van Pd, Ru, Tc, Nb, Mo, Zr, ens, wat geproduseer is deur 400 MeV ^{16}O- en ^{12}C-geïnduseerde reaksies met Rh in $RhCl_3.3H_2O$ skywe. 5% ammoniak-

oplossing is gebruik om die Pd uit die hars te elueer, met 'n herwinning van 92%.

Om die saadjies vir implantering te maak, is ^{103}Pd op 'n matige basiese anioonuitruilerhars Amberlite IRA-93 gesorbeer deur 'n ^{103}Pd-oplossing, in 0.5 M HCl, deur 'n 0.5 ′ 1cm kolom te hersirkuleer vir 2 uur. 'n Tregter is ontwerp om die ^{103}Pd-gelaaide harskorrels oor te dra na die titaanbuisies (0.7 mm binnedeursnit, 0.8 mm buitedeursnit en 4.5 mm lank). Om die buisies te verseël, is dekseltjies uit 'n 0.02 mm titaanplaat gesny. Verskeie dekseltjies is gemasjieneer om op die buisies vas te sweis. 'n Punt-sweismasjien is gebruik vir die sweiswerk nadat geringe, maar belangrike, aanpassings aan die masjien gedoen is.

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CHAPTER 1

MOTIVATION, AIMS AND GENERAL BACKGROUND

1.1. MOTIVATION AND AIMS

Prostate cancer is the most common cancer found in men in the USA today. In 1997 there were 240,000 newly discovered cases and about 40,000 deaths [1]. These numbers have started to drop as the result of the development of a screening test, Prostate Specific Antigen (PSA), and much improved public awareness of the importance of seeking evaluation at a regular schedule.

Of all the treatment options for men with organ-confined prostate cancer, brachytherapy – permanent implantation of radioactive seeds into the prostate gland – is the least disruptive for the patient, both physiologically and practically [2]. Treatment decisions will continue to be made on the basis of patient and physician preferences in conjunction with clinical probabilities. Long-term results in this series show that monotherapy with seed implants achieved disease-free survival of 66% of patients; moreover, 79% of patients with higher grade disease who were treated by a combination of brachytherapy and external beam radiation also experienced long-term disease-free survival [3].

Permanent implantation of tumours by radiation seeds is an established technique for treatment of several tumour sites such as the prostate [1]. Recently, permanent implants of the prostate have become increasingly popular with the development of a transperineal percutaneous implantation technique under transrectal ultrasound and template guidance, which can be an outpatient procedure in a 1-day surgery unit (see also section 1.1.6.4). Because of the low energy of photons emitted by encapsulated sources of ^{125}I (27 keV, average), the ^{125}I sources are well-suited for permanent

implants from the point of view of radiation exposure of persons around the patient during the procedure and after release from the hospital. The half-life of ^{125}I, however, is long (60 days) for a permanent implant, resulting in highly protracted continuous low dose rate irradiation. Typical ^{125}I implants are planned to deliver a dose of 160 Gy to full decay. The initial dose rate is 77.2 mGy/h and 87.5% of the full dose is delivered over a period of 6 months (three half-lives) [4,5].

It is well known that the biological effectiveness of radiation decreases with decreasing dose rate because of repair of sublethal and potentially lethal damage, recruitment of relatively quiescent subpopulations of cells, and repopulation of target cell population itself. In the dose rate range of permanent ^{125}I implants (77.2 mGy/h and less), it has been argued that for a 5-day cycle time, ^{125}I implants should be more effective than external beam radiation. Using similar arguments, one can conclude that for ^{125}I permanent implants, the dose rate is so low that tumour cells that have cycle times of 2-5 days cannot be effectively killed by this low dose rate irradiation. ^{103}Pd sources were developed to overcome this problem. ^{103}Pd sources emit on average 21 keV photons and have a half-life of 17 days. Because of the low energy of photons emitted by ^{125}I and ^{103}Pd, both of these sources offer the considerable advantages of easy and effective radiation shielding of patient and personnel, compared to other sources used for permanent implants, such as ^{198}Au and ^{222}Rn. Because of its shorter half-life, the ^{103}Pd implants offer initial dose rates of about 2.5 times larger than the ^{125}I implants. This higher dose rate is believed to offer a potential advantage over ^{125}I implants, which have had somewhat disappointing results for more aggressive and rapidly proliferating tumours. Also, the lower energy of photons emitted from ^{103}Pd compared to ^{125}I reduces the risk of complications arising from irradiation of normal tissues outside the tumor volume, because the dose rate outside the ^{103}Pd implants falls off more rapidly than outside ^{125}I implants.

Because of the lower energy of ^{103}Pd and the fact that the attenuation coefficients increase rapidly with decreasing photon energy - approximately by the cube of photon energy in the range 30 to 20 keV - there was a concern that the penetrating ability of ^{103}Pd photons may not be adequate for conventional seed configurations used in interstitial brachytherapy. In other words, one may obtain cold spots in the implanted volume if the geometric configuration of the seeds is identical to that for ^{125}I implants.

A dosimetry study by Meigooni *et al.* [4,5], however, on both implants showed that: (a) within the tumour volume, the isodose distributions produced by ^{103}Pd are very similar to those of ^{125}I and outside the tumour volume those for ^{103}Pd fall off more rapidly; (b) dose uniformity in the tumor volume is essentially the same for ^{103}Pd and ^{125}I implants of the same geometry and (c) source strength for a ^{103}Pd implant delivering 115 Gy should be about 3.3 times that for an ^{125}I implant delivering 160 Gy with the ratio of source strengths greater for larger implants.

Since 1987, encapsulated sources of ^{103}Pd have been introduced as an alternative to conventional brachytherapy sources of ^{125}I. With a half-life of 16.97 days, ^{103}Pd delivers 95% of its dose over eight weeks [6] providing improved control of rapidly proliferating tumours and a more rapid clinical response of lesions.

Although ^{103}Pd has been used for various kinds of cancers [6,7], it has almost exclusively been the method of choice for prostate cancer, the most common cancer with the highest death rate.

Two different routes for production of ^{103}Pd by cyclotron are used. One involves proton bombardment of a ^{nat}Ag target, employing a high-energy cyclotron (*ca* 66 MeV cyclotron – at iThemba LABS, South Africa) [8]. The other route makes use of low energy proton or deuteron bombardment (next section) of ^{nat}Rh targets [9,10,11,12]. For the latter, therefore, a 30 MeV compact cyclotron is very well suited. At iThemba LABS (previously NAC), a Ag target is made of 16 g highly pure granular silver pressed to a 2 cm-diameter tablet. For the second route, the Rh target can be made from pure metal (as a sheet or lump) [13] or by electroplating Rh on a copper substrate. At present, several countries have a 30 MeV cyclotron (such as one manufactured by the IBA company, Belgium) which employs a special designed copper substrate for the target [9]. Since the final product of ^{103}Pd is to remain as a permanent implant in the body of the patient, it must have as low level of radionuclide impurities as possible to prevent extra radiation exposure. This is more crucial when high-energy, long-lived radioisotopes are involved. The radiochemistry of ^{103}Pd from a Ag target includes the separation of Pd from large amounts of Ag (the target material) and radioisotopes of Rh, (mainly daughters of their Pd isotopes) such as ^{100g}Rh (from ^{100}Pd decay) and ^{101}Rh (from ^{101}Pd decay).

The pure ^{103}Pd obtained from the radiochemical separation must then be loaded into the small-sized Ti tube (a biocompatible material) and sealed, preferably by welding.

One of the ^{103}Pd seed models, which has been exclusively used in recent years, contains two rectangular ^{103}Pd -plated graphite pellets separated by a rectangular lead X-ray marker (1.0 mm × 0.5 mm) [6,7]. The dimensions of the pellets are 0.9 mm × 0.6 mm. Considering the 0.7 mm inner diameter of the titanium tube, the thickness of each graphite pellet must be 0.3 mm or less to be able to move through the Ti tube easily.

In this study, sorption of the final product of ^{103}Pd on an anion exchange resin, followed by transferring the resin beads into the Ti tubes, was considered for the first time.

To develop a separation technique for a new radionuclide production, several routes had to be studied and many experiments performed to find the best one in terms of the recovery of the radionuclide of interest, chemical and radionuclide impurities in the final solution, speed of procedure, the volume of solution for the separation and ease with which the procedure can be achieved in the hot cell. Before any radiochemical separation in a hot cell can be done, experiments have to be performed with natural elements ("cold run"). The selection of a measurement procedure and technique has to be compatible with the instruments available at the particular laboratory.

The world demand for ^{103}Pd seed is much higher than the present production. For countries having cyclotrons it is more profitable and convenient to produce ^{103}Pd to satisfy their national demand.

It must be mentioned that the elements involved in this study are normally written in the form of their chemical symbols, regardless of their ionic forms, oxidation states, different isotopes or complexes – although the media in which they are dissolved allow for each element to maintain their most stable oxidation states (I, II, III and II for Ag, Cu, Rh and Pd, respectively). While a thorough speciation investigation of

the elements of interest falls outside the scope of this work, some discussion is included to explain their ion exchange behaviour in the different media used in this study.

The main objectives of the investigation can therefore be summarised as follows:

1. To develop a radiochemical method, based on anion exchange chromatography, for the separation of ^{103}Pd from Ag targets to either produce " ^{103}Pd seeds " for brachytherapy, or for exporting the pure activity as a solution. This comprises the separation of ^{103}Pd (and maximum 1 mg natural Pd as carrier) from 16 g Ag and from isotopes of Rh produced in the nuclear reaction and the decay of their Pd parents.

2. To achieve the radiochemical separation routinely in a hot cell and to design an easily operated radiochemical processing system.

3. To find a method for the preparation of a Rh target by electroplating rhodium on a pure copper substrate, the dissolution of the electroplated Rh by an alternating current and to design an electrolysis cell to perform both electroplating and electrodissolution steps.

4. To determine the distribution coefficients of Pd, Rh and Cu on the weakly basic anion exchange resin Amberlite IRA-93 at different HCl concentrations: firstly to find the optimum concentration of HCl for possible separation of Pd from Rh and Cu and, secondly, to obtain the best concentration for the sorption of ^{103}Pd as an alternative method for the production of ^{103}Pd seeds.

5. To develop a procedure, based on ion exchange chromatography, for the separation of carrier-free ^{103}Pd from Rh targets.

6. To produce ^{103}Pd seeds using: (a) spherical anion exchange resin beads, instead of graphite pellets, for the sorption of ^{103}Pd and (b) to modify an inexpensive spot-welding machine, instead of using very expensive electron-beam equipment, for sealing the Ti tubes (as the seed).

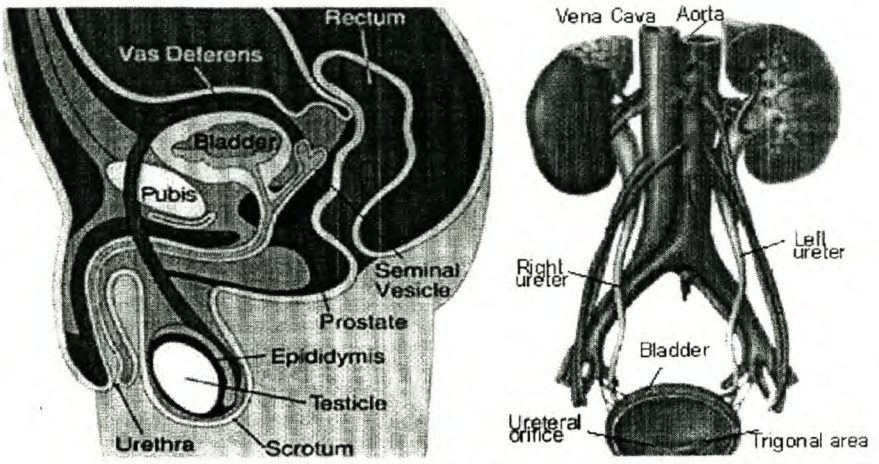
1.2 PROSTATE CANCER AND BRACHYTHERAPY

After a brief historical review of prostate brachytherapy, anatomy, some diagnostic procedures, rationale for treatments, patient selection criteria, up-to-date implant techniques, long-term (about 14-year) outcome results and comparison of ^{103}Pd with ^{125}I are discussed in this chapter.

1.2.1 Prostate: Anatomy and Function

The prostate is a walnut-shaped gland, about one and a half inches long. The prostate gland lies deep in the pelvis, directly beneath the bladder [14]. It completely surrounds the urethra, the channel running from the bladder through the penis, which carries both urine and semen from the body (Fig.1.2.1) [3,15]. It is just in front of the rectum so that part of the gland may be easily examined by a simple Digital Rectal Examination, DRE (see next section for the definition). In young men it is usually the size of a walnut, but may grow with age to the size of a lemon, or sometimes even larger.

The primary function of the prostate gland is to produce part of the fluid that makes up semen. During ejaculation, muscles in the prostate contract to push the prostatic fluid through tiny ducts into the urethra, where it mixes with sperm and other fluid [15]. Some urologists believe, however, that it supports the ejaculatory ducts, or sperm tubes, but appears not to have any other function in human [14].



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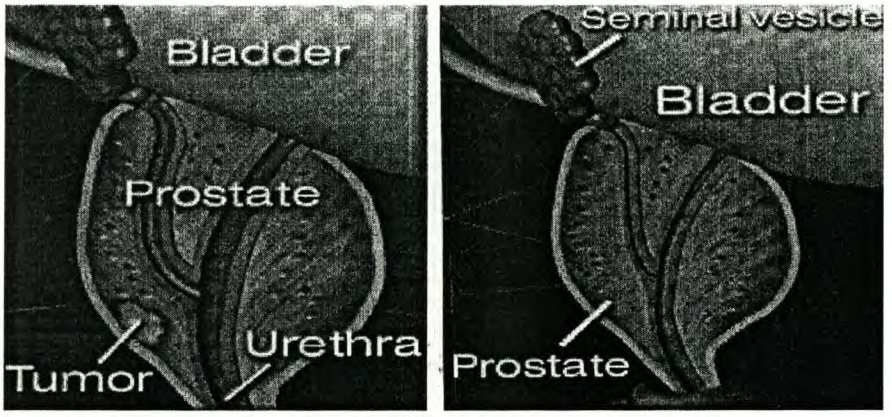

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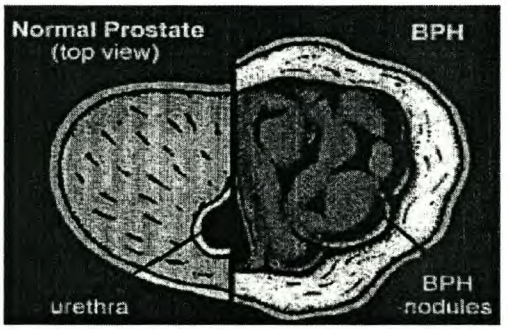

(c)

Fig.1.2.1. (a) anatomy of prostate related to other organs; (b) normal and tumorous prostates; (c) comparison of normal with BPH nodules.

1.2.2 Symptoms and diagnosis

Prostate cancer usually exists without symptoms. Some patients may have symptoms of having to urinate frequently or slowly, or have urinary burning or blockage or bleeding. These symptoms usually come from other conditions such as infection or inflammation or overgrowth, but may be associated with prostate cancer. When these symptoms occur the patient should seek urologic evaluation. When the cancer has spread, bone pain is a common symptom [14].

All men over 50 and below 80 should have an annual prostate cancer examination. And men over 40 with strong family histories, (fathers, brothers or any two close relatives), and all African-American men over 40 should have an annual exam. In those few families with multiple males having had prostate cancer screening might be considered at an earlier age [14]. Prostate cancer is very common in men over 80, but is usually a slow growing, non-life threatening disease. Men over 80 should have an annual DRE for prostate and colorectal examination, and if the prostate is abnormal a PSA may be obtained (see also below) [15,3].

1.2.3 The prostate examination

The prostate examination consists of two parts, a digital rectal examination (DRE), and a blood test for prostate specific antigen (PSA). The combination of the two examinations significantly increases the detection of prostate cancer over either test alone [14].

The DRE is performed by the examiner by gently inserting a gloved-finger into the rectum and palpating the gland for size, shape, consistency, and nodules or lumps. The examiner may also check for colon or rectal cancer or other conditions. Prostate nodules should not be ignored. Although about half of prostate nodules found will not be cancerous[14,15], the examiner cannot tell from the examination alone whether cancer is present. Some prostate cancers cannot be felt by DRE because they lie in a

part of the gland that the finger cannot reach, or they are too small to feel or they just do not feel abnormal. All nodules require further evaluation.

PSA is a substance made by prostate cells and is measured in nanograms per millilitre of blood [14]. It is a blood test that helps detect prostate cancer. PSA is a fuzzy test and cannot diagnose prostate cancer by itself. Many other conditions such as prostate infection or inflammation, or urinary tract infection may raise the PSA. The other factor that can elevate PSA levels is BPH (noncancerous disorder Benign Prostatic Hyperplasia; see also Fig. 1.2.1) [15], a benign condition, which is common in older men. A high PSA does not mean cancer is present and a normal PSA does not rule out the presence of prostate cancer. The normal values for PSA are 0 to 4. Borderline levels are 4 to 10 and when it is over 10 it is considered high.

When the levels are between 4 and 10 a second fuzzy blood test, the Total vs. Free PSA ratio may be helpful. While high ratios, over 25%, suggest benign disease, and low ratios, under 15%, suggest cancer, there are many false positive and negative results, and the evaluation of the results are best left to a urologist. This test is not valid for PSA' s less than 4 or greater than 10.

Sometimes when the PSA is borderline or elevated, or a nodule is present, and there are symptoms suggestive of infection or inflammation, the urologist, (this decision is best left to an expert), may decide to treat the condition with antibiotics for 2 to 4 weeks and repeat both the PSA and the examination. If both examinations return to normal, cancer is usually not present, and a repeat examination in 3 to 6 months is indicated.

In addition to the PSA and DRE, the physician may order an ultrasound of the prostate. By imaging the prostate with ultrasound, the physician may be able to locate cancer that the other tests did not detect. If the ultrasound image suggests cancer, the physician can place a needle into the prostate to take a biopsy.

A biopsy is a surgical procedure in which a tissue sample is taken. It can be taken in the office or hospital. The tissue sample is sent to the laboratory for diagnosis. Multiple samples are taken in different areas of the prostate to minimise the

possibility of missing cancer. Most patients report minimal, if any, discomfort. If the biopsy indicates cancer, the doctor then "stages" the tumour based on which biopsy specimens contain cancer, the extent of cancer, and the location of cancer in the specimens. Staging also depends on the extent and location of cancer outside the confines of the prostate.

1.2.3.1. Stages of prostate cancer

The Stage of a cancer refers to how far it has progressed and gauges the severity of cancer on an escalating scale. There are several different staging systems, but the most commonly used are ABCD [14] and TNM (Tumour, Nodes, Metastases), which has largely replaced the ABCD system [15]. Within each stage there are sub-stages.

ABCD System

Stage A describes a cancer that is only found by elevated PSA and biopsy, or at surgery for obstruction. It is not palpable on DRE. It is localised to the prostate. This type of cancer is usually curable, especially if it is a relatively low Gleason grade (next section).

Stage B cancer refers to a cancer that can be felt on rectal examination and is limited to the prostate. Other tests, such as bone scans or CT/MRI scans, may be needed to determine this stage, especially if the PSA is significantly elevated or the Gleason grade is 7 or greater. Many Stage B prostate cancers are curable.

Stage C cancer has already spread beyond the capsule of the prostate into local organs of tissues, but has not yet metastasised or jumped to other sites. This stage is determined by Digital Rectal Exam, or CT/MRI scans, and/or Sonography. The bone scan, and, if done, the Prostascint scan are negative. Some Stage C cancers are curable.

Stage D cancer has already spread, usually to distant lymph nodes, bones or other sites. This is usually determined by bone scan, Prostascint scan or other studies. Stage D is not curable but is treatable.

TNM System

Stage T1: The tumour is microscopic and confined to the prostate, but is undetectable by a digital rectal exam (DRE) or by ultrasound. It is usually discovered by PSA tests or biopsies.

Stage T2: The tumour is confined to the prostate and can be detected by DRE or ultrasound.

Stage T3 or T4: In stage T3, the cancer has spread to the tissue adjacent to the prostate or to the seminal vesicles. Stage T4 tumours have spread to organs near the prostate, such as the bladder.

Stage N+ or M+: Cancer has spread to pelvic lymph nodes (N+) or to lymph nodes, organs, or bones distant from the prostate (M+).

1.2.3.2. Grading of prostate cancer

When urologists discuss cancer diagnosis with their patients they often talk of a Gleason Grade with reference to the degree of aggressiveness of a particular tumour. This grade imparts a significant correlation to the potential prognosis and is an important factor in recommending a particular therapy for that patient. The following is a brief description of the scoring technique and its relevance [16].

Gleason Grades1 and 2: These two grades closely resemble a normal prostate. They are the least important grades because they seldom occur in the general population and because they confer a prognostic benefit which is only slightly better than grade 3. Both of these grades are composed of very pale glands which grow closely together. In grade 1 they form a compact mass; in grade 2 they are more loosely aggregated, and some glands wander (invade) into the surrounding muscle (stroma).

Gleason Grade3: This is the most common grade and is also considered well differentiated (like grades 1 and 2). This is because all three grades have a normal "gland unit" like that of a normal prostate; that is, every cell is part of a circular row which forms the lining of a central space (the lumen). The lumen contains prostatic secretion like normal prostate, and each gland unit is surrounded by prostate muscle

which keeps the gland units apart. In contrast to grade 2, wandering of glands (invading) into the stroma (muscle) is very prominent and is the main defining feature. The cells are dark rather than pale and the glands often have more variable shapes.

Gleason Grade 4: This is probably the most important grade because it is fairly common and because of the fact that if a lot of it is present, patient prognosis is usually (but not always) worsened by a considerable degree. There is also a big jump in loss of architecture. For the first time, we see disruption and loss of the normal gland unit. In fact, grade 4 is identified almost entirely by loss of the ability to form individual, separate gland units, each with its separate lumen.

Gleason Grade 5: Gleason grade 5 is an important grade because it usually predicts another significant step towards poor prognosis. Its overall importance for the general population is reduced by the fact that it is less common than grade 4 and it is seldom seen in men whose prostate cancer is diagnosed early in its development. This grade too shows a variety of patterns, all of which demonstrate no evidence of any attempt to form gland units. Although never an absolute the results with any form of conventional therapy is poor with this category.

The combined Gleason score or Gleason sum: When a pathologist looks at prostate cancer specimens under the microscope and gives them a Gleason Grade, he or she will always try to identify two architectural patterns and assign a Gleason Grade to each one. There may be primary patterns and then a secondary pattern which the pathologist will seek to describe for each specimen; alternatively, there may often be only a single pure grade.

In developing his system, Dr. Gleason discovered that by giving a combination of the grades of the two most common patterns he could see in any particular patient's specimens, he was better able to predict the likelihood that that particular patient would do well or badly. Even though it may seem confusing, the Gleason score which a physician usually gives to a patient is actually a combination or sum of two numbers. These combined Gleason sums or scores may be determined as follows:

The lowest possible Gleason score is 2 (1+1), where both the primary and secondary patterns have a Gleason Grade of 1, therefore, when added together their combined sum is 2. Typical Gleason scores might be 5 (2+3), where the primary pattern has a Gleason grade of 2 and the secondary pattern has a grade of 3, or 6 (3+3), a pure pattern. Another typical Gleason score might be 7 (4+3), where the primary pattern has a Gleason grade of 4 and the secondary pattern has a grade of 3. Finally, the highest possible Gleason score is 10 (5+5), when the primary and secondary patterns both have the most disordered Gleason grades of 5.

The grade of a prostate cancer specimen is very valuable to doctors in helping them to understand how aggressive the prostate cancer is by determining how fast it is growing and how it is spreading and how a particular case of prostate cancer can be treated. In general, the time for which a patient is likely to survive following a diagnosis of prostate cancer is related to the Gleason score. The lower the Gleason score, the better the patient is likely to do. It should be remembered, however, that prostate cancer is a very complicated disease. People with low Gleason scores have been known to fare poorly and men with high Gleason scores have been known to do well. General principles do not always apply to individual patients.

The higher the numbers when the two are added, the more aggressive the tumour is likely to be. A score of 2 to 4 (low) means the cancer looks approximately normal and is probably slow growing. A score of 7 to 10 (high) means the cells look abnormal and are probably growing quickly.

1.2.4 Treating the disease

Armed with diagnostic data, patients and their doctors must then decide on a treatment course. It is at this point that patients must be well educated. The decisions made on treatment are so crucial and will have such an effect on quality of life, men must weigh them very carefully. They must also remember to include their partners in the decisions because they will be affected by the course of action too [15]. The choice of what type of therapy is appropriate for a patient with prostate cancer: radical prostatectomy, radiation, seeds, combined therapy, observation or watchful waiting,

cryotherapy or hormonal therapy, is dependant on many factors including: the Gleason Grade and the Stage of the cancer, the patient's age, the patients medical condition and the patient's desires. There is no absolutely right or wrong way to treat every patient, and what is appropriate for one patient may not be so for another [14].

In general prostate cancer tends to be less aggressive with increasing age of onset. Indeed, prostate cancer discovered when the patient is over 80 years of age tends to be slow growing and is usually observed or watched and treated only if the cancer seems to be growing aggressively. Similarly, patients with other severe medical conditions who are discovered to have prostate cancer may be best observed, and treated only if the prostate cancer is aggressive. Some patients with lower grade, (Gleason 2 –5) or very small amounts of cancer found in the gland may elect observation. The risk of developing metastases and incurable disease must be balanced against the desire to avoid treatment.

Younger, healthy prostate cancer patients with curable disease, Stage A, Stage B, and some early Stage C, should be treated aggressively with either surgery, or varied forms of radiation, such as conformal external beam, seed implantation, (brachytherapy), combined therapy, or possibly with cryotherapy. Over the long run, surgery provides a slightly better chance for cure and should be favoured on younger healthier patients. In some cases where there is a high suspicion of local spread: Stage C, or Gleason grade 7 or 8, or a PSA over 10, surgery followed by radiation with or without hormone therapy may be indicated [14].

Patients aged 70 to 79 or patients with other serious, life threatening diseases, should be treated with one of the forms of radiation therapy, cryotherapy, or in some cases, observation.

Sometimes, combined therapy, short term hormonal treatment, used in combination with radiation treatments is appropriate.

Historically, prostate cancer patients with advanced cancer: Stage D, or extensive Stage C, disease were best treated with hormonal therapy. While not curing prostate cancer, hormonal therapy frequently slows its course and prolongs life and comfort.

Recent research, however, suggests that aggressive treatment of the local cancer, with surgery or combined hormone therapy, external beam irradiation and seeds, plus long term hormonal suppression significantly increases life expectancy and cancer free survival. This is a major change in therapy.

Patients with Gleason grade 8, 9 or 10 have very poor cure rates and, indeed, may not benefit from surgery or radiation. Treatment is controversial. Some urologists will perform surgery for these high grades and give long term hormones. Others will not offer any conventional treatment as the results are poor.

Surgery (or Prostatectomy) is a very common-operation. About 200,000 of these procedures are carried out annually in the U.S. A prostatectomy for benign disease (BPH) involves the removal of only the inner portion of the prostate (simple prostatectomy). This operation differs from a radical prostatectomy for cancer, in which all prostate tissue is removed. Simple prostatectomy offers the best and fastest chance for improving BPH symptoms, but may not totally alleviate discomfort. For example, surgery may relieve the obstruction, but symptoms may persist due to bladder abnormalities [1].

Surgery is also associated with the greatest number of long-term complications including impotence, incontinence, retrograde ejaculation (ejaculation of semen into the bladder rather than through the penis) and the need for a second operation (in 10% of patients after five years) due to continued prostate growth or a urethra stricture resulting from surgery. While retrograde ejaculation carries no risk, it may cause infertility and anxiety. The frequency of these complications depends on the type of surgery.

Surgery is delayed until any urinary tract infection is successfully treated and kidney function is stabilised (if urinary retention has resulted in kidney damage). Men taking aspirin should stop taking the drug 7 to 10 days prior to surgery, since aspirin interferes with the blood's ability to clot. Transfusions are required in about 6% of patients after TURP and 15% of patients after open prostatectomy (see next paragraphs).

Since the timing of prostate surgery is elective, men who may need a transfusion - primarily those with a very large prostate who are more likely to experience significant blood loss - have the option of donating their own blood in advance, in case they need it during or after surgery. This option is referred to as an autologous blood transfusion.

Transurethral prostatectomy (TURP) [1] is considered the "gold standard" of BPH treatment - the one against which other therapeutic measures are compared. It involves the removal of the core of the prostate with a resectoscope - an instrument passed through the urethra into the bladder.

Improvement after surgery is greatest in those with the worst symptoms. Marked improvement occurs in about 93% of men with severe symptoms and in about 80% of those with moderate symptoms. The mortality from TURP is very low (0.1%); however, impotence follows TURP in about 5 to 10% of men and incontinence occurs in 2 to 4%.

Transurethral incision of the prostate (YUIP) was first used in the U.S. in the early 1970s. Like TURP, it is done with an instrument that is passed through the urethra. Instead of removing excess tissue, the surgeon only makes one or two small cuts in the prostate with an electric knife or laser. These incisions relieve pressure on the urethra. TUIP can only be done on men with smaller prostates. It takes less time than TURP and can be performed on an outpatient basis under local anaesthesia in most cases. A lower incidence of retrograde ejaculation is one of its advantages.

Open prostatectomy is the operation of choice when the prostate is very large – e.g. >80 grams - since transurethral surgery cannot be performed safely in these men. It carries a greater risk of life-threatening complications in men with serious cardiovascular disease, however, since the surgery is more extensive than TURP or TYIP.

In the past, open prostatectomies for BPH were carried out either through the perineum (the area between the scrotum and the rectum) - called perineal prostatectomy - or through a lower abdominal incision. Perineal prostatectomy has

largely been abandoned for the BPH due to the higher risk of injury to surrounding organs, though it is still used for prostate cancer. Two types of open prostatectomy for BPH - suprapubic and retropubic – employ an incision extending from below the umbilicus (navel) to the pubis. A suprapubic prostatectomy involves opening the bladder and removing the enlarged prostatic nodules through the bladder. In a suprapubic prostatectomy, the bladder is pushed upward and the prostate tissue is removed without entering the bladder. In both types of operation, one catheter is placed in the bladder through the urethra, and another through an opening made in the lower abdominal wall. The catheter remains in place for three to seven days after surgery. The most common immediate postoperative complications are excessive bleeding and wound infection (usually superficial). More serious potential complications include heart attack, pneumonia, and pulmonary embolus (blood clot to the lungs). Breathing exercises, leg movements in bed, and early ambulation are aimed at preventing these complications. The recovery period and hospital stay are longer than for transurethral prostate surgery.

External adiation gives poor results. There are several different forms of radiation therapy: external beam, several forms of combined therapy, high dose interstitial radiation and brachytherapy or seed implantation. The last two techniques will be discussed in more detail in the following pages (under Brachytherapy).

External beam therapy is administered as an outpatient over a 5 to 7 week period. Usually five treatments, lasting several minutes, are given weekly. Several different "ports" are used so that the tissues surrounding the prostate get less radiation than the cancer. Frequently the patient will feel very tired during the later stages of radiation, and temporary or long term bladder or bowel irritability may occur. Impotence eventually occurs in about 50% of those receiving radiation treatment, but incontinence is rare unless there has been prior prostate surgery. The results, in terms of cure, are similar to surgery for about 10 years, but after that time surgical treatment shows a slight advantage. There are several varieties of external beam radiation, such as conformal, rotational or wide field, the discussion of which is better left to the radiation oncologist [14,15].

Combined therapy has many different meanings to different people. It may refer to combined external beam and brachytherapy, or combined hormonal and radiation therapy. The various therapies are an attempt to improve the long term results of therapy. These various forms of therapies are used in selected patients, such as those with extensive cancer in the prostate or a high likelihood of local extension, i.e. stage C disease.

Neoadjuvant combined therapy combines a form of radiation with short term hormonal therapy. In many centres, hormone therapy with LHRH is started at least two months before radiation is started and continued for two months after radiation therapy is completed. Hormonal therapy kills many cancer cells and weakens many others, perhaps increasing the efficiency of the radiation therapy. Long term data is not available at the present but this combination is suggested to patients undergoing all forms of radiation therapy. Early aggressive hormonal therapy may be the appropriate way to treat these few patients.

There is no one way to treat any one patient, and a discussion with the urologist, is necessary to arrive at an appropriate treatment plan [14,15,2,3].

1.2.5 Follow-up, on going care, and recurrence

Prostate cancer requires lifelong follow-up [14]. Unfortunately, prostate cancer can recur many years after apparently successful treatment. There have been recurrences after 10 to 15 years, so a patient who has had prostate cancer must get regular check-ups through their life. There are two different sites of recurrence, locally in the prostate bed and metastatic to other sites.

A prostate cancer follow-up visit will include a review of the symptoms such as changes in voiding patterns, bleeding, weight-loss and bone pain. A digital rectal exam, DRE, will be performed to determine if there are any changes in the prostate or prostate bed, and a PSA obtained to see if there are any increases that should be investigated.

In general, when there are no signs of recurrence, follow-ups should be every 3 months for 1 to 3 years, every six months for several years and after 5 years no less than once a year. Factors such as Gleason Grade, extensiveness of the cancer, and whether it is confined to the prostate.

Normally after radical prostatectomy, the PSA will drop to less than 0.1, although some laboratories only test to less than 0.2. Failure to drop to this level is cause for concern and further evaluation or treatment may be necessary. The DRE tells the urologist if there are any changes in the surgical site, and the appearance of a lump or thickening in the prostate bed also requires further evaluation. Not all rises in PSA or changes in the DRE are recurrent cancer, there might be regrowth of a small amount of normal prostate tissue, but this must be proven. If there is a slight rise in PSA, a repeat blood test in several weeks or months may be appropriate, especially if there is a low probability of recurrence, that is, if the Gleason grade was less than 7 and the cancer was confined to the prostate at surgery. Otherwise, a sonogram and biopsy, and a bone scan, or possibly a Prostascint scan may not be needed before secondary therapy is started.

When the cancer recurs only in the prostate bed, a secondary cure with radiation or cryotherapy may be achieved in some patients. Others will develop progressive disease. If the only sign of recurrence is a rising PSA without any detectable disease, some physicians will recommend local radiation, others hormonal therapy and others will observe it until the site of recurrence is obvious. There is no one correct answer and the treatment decision will lie with the doctor and the patient [14,15,17,18,3].

1.2.6 Prostate brachytherapy

"Brachy" is a Greek prefix meaning "short" (just as "tele" means long). Brachytherapy is a treatment at short range, as contrasted, for example, with being bombarded at a distance by external beam radiation (EBR). In prostate brachytherapy radiation comes from small radioactive "seeds" implanted very close to the area being

treated. This minimises the chance of affecting nearby tissue while still delivering enough radiation to the prostate to destroy the cancerous cells [19].

The last decade has seen remarkable growth in a form of prostate radiation therapy called brachytherapy or seed implantation, where tiny radioactive sources are implanted transperineally into the prostate gland. Increasingly, the procedure is playing a major role in the treatment of clinically localised prostate cancer. Indeed, analyses of Medicare data show that brachytherapy is apparently replacing radical prostatectomy as the treatment of choice for early-stage prostate cancer [1,2].

Brachytherapy is considered to have several advantages over radical prostate surgery [2]. These include:

1. It is a simple, cost-effective outpatient procedure that can typically be performed in less than one hour.
2. It is a minimally invasive procedure requiring no incisions or sutures.
3. The anaesthesia of choice is spinal, making prostate brachytherapy safer for men who may be considered at increased risk for general anaesthesia.
4. Bleeding is generally unworthy of notice.
5. Recovery is rapid, allowing most men to return to work or resume usual activities within a day or two. In contrast, men who undergo radical prostatectomy require weeks of recovery.
6. Lifestyle changes, frequently required after a radical prostatectomy, are uncommon after a seed implant.

When compared with external beam radiation therapy, the spatially controlled radiation deposited by modern brachytherapy is considered to have the following advantages [20]:

1. Using real-time ultrasound imaging, radiation sources can be placed safely and accurately, ensuring that the therapeutic dose delivery is confined to the prostate gland.
2. The low-energy radioactive sources, such as Pd-103 or Iodine-125, have limited tissue penetration. This allows for a sharp drop-off of the radiation dose at the edge of the gland, limiting radiation delivery to normal tissues and minimising potential treatment-related complications.

3. Prostate gland movement that can significantly affect the accuracy of external beam therapy and compromise both prostate and normal-tissue doses is generally not a factor during implantation with real-time ultrasound imaging.
4. Radiation exposure to physicians, nursing personnel, and family members is negligible.
5. A single outpatient treatment for placement of an implant as monotherapy is convenient, taking little of the patient's time compared with a protracted seven-week course of external beam radiation.
6. The precision and conformation of the brachytherapy dose to the gland allows for administration of a radiation dose roughly 50% to 100% greater than that which can be safely delivered by conventional or conformal external beam therapy. This is especially important, as increasing evidence shows that local tumour control improves with the amount of radiation delivered.
7. Taken together, the advantages of brachytherapy compared with other treatments for prostate cancer are substantial. This section provides a brief historical review of prostate brachytherapy, rationale for treatments, patient selection criteria, description of current implant techniques, and long-term (15 –year) outcome results.

1.2.6.1 History

Brachytherapy of the prostate goes back to 1911 when the first case in medical literature published. Utilising a technique, which is rather crude by today's standards, simply used a catheter to insert Radium-226 into the prostatic urethra. Although the results showed fairly good local control of the cancer, the complications were too high to be considered acceptable. This early technique of brachytherapy represents the oldest technique for delivering radiation to the prostate gland, preceding external beam therapy or the prostate by several decades, and antedating modern prostate cancer surgery [2,18].

In 1915, at New York's Memorial Hospital (now Sloan Kettering Cancer Centre), Radium needles were inserted into the prostate. The procedure was described as follows: "these needles are 4-6 inches long and are inserted through the perineum into the prostate of further into the vesicles. A finger in the rectum is used to guide the

needles." It was concluded that, "Early cases showed a marked regression of the prostatic lump and in some cases complete disappearance of these."

In 1950's and 1960's, at University of Lowa, a solution of colloidal radioactive Gold-198 was injected into the prostate glands of patients with inoperable prostate cancers. Although the results in a large number of patients suggested low mortality and morbidity, the technique was not widely used. Around the same time period, a combination of external beam radiation and Gold-198 seed implantation for advanced prostate cancers was used.

Open implant techniques

Real interest in prostate brachytherapy did not occur until the 1970's when an open implant technique was described using the radioisotope I–125. The isotope was contained in miniature, sealed titanium cylinders tailored to fit into and be administered by needles. The implant needles holding the I-125 seeds were inserted "free-hand" into the prostate without any imaging device for guidance, while the index finger of one of the operator's hands was in the rectum to help verify the needle depth.

The open implant procedure had great appeal. Conceptually, a highly confined dose of radiation was delivered to the prostate gland, sparing the juxtaposed bladder and rectum from undue radiation damage. But, free-hand needle and seed placements all too often resulted in inconsistent close distributions not recognised or appreciated until post-operative imaging was performed. Consequently, some areas of the gland received more radiation than planned ("too hot") while other areas received less radiation than intended ("too cold"). The "too hot" segments often led to serious complications, while often the sublethal radiation delivered to the "too cold" areas resulted in a high rate of local failure. This method did not gain wide acceptance due to less than satisfactory clinical results and various complications. Moreover, some investigators incorrectly advocated brachytherapy for patients with bulky, advanced lesions that were incurable with any therapy, which confounded already variable results.

In the late 1960's, was the beginning of treatment of prostate cancer with newly emerging, megavoltage external beam radiation technology. It was demonstrated that external radiation therapy could cure prostate cancer by the delivery of high doses of radiation to the prostate gland. This form of radiation and newly developed technique of removing the prostate surgically soon became the preferred treatments for prostate cancer; interest in prostate brachytherapy gradually declined [18,2].

These early failures, to a large degree, were due to the fact that they were performed utilising "blind" approaches. The imaging technologies, crucial for seed implantation, were not yet available. Precise placement of seeds is a crucial factor in the success of brachytherapy. Without the benefit of modern day imaging techniques accurate placement of the radioactive seeds was not attainable.

In the early 1980s, the old concept of brachytherapy was revisited. Improved imaging technologies made the procedure more feasible. The most important of these were transrectal ultrasound (TRUS) and computerised tomography (CT). In 1983, a technique of implanting the prostate gland with radioactive seeds transperineally was introduced. The seed-bearing needles were guided into precise positioned in the prostate gland by transrectal ultrasonography. This novel and elegant technique has been shown to be generally reproducible and yielded clinically meaningful results.

In 1985, Ragde performed the first prostate seed implantation in the U.S at Northwest Hospital in Seattle [2]. Two years later, he performed the first Pd-103 implantation for prostate cancer and established a national brachytherapy implant course. His unswerving commitment to development of this modality, namely radioactive seed implantation for treatment of prostate cancer, as well as dedication to the training of other physicians in the technique, soon led to a resurgence of interest in prostate brachytherapy. These new technologies allowed a non-surgical, uniform seed distribution into the prostate through needle punctures. With the most recent developments in computer software, TRUS has become the most commonly used modality for seed implantation procedures. The results, however, can be highly operator-dependent [2,18].

1.2.6.2 Current brachytherapy technique

The technique of prostate seed implantation represents - even in the era of advanced radiotherapy techniques, such as three-dimensional conformal radiotherapy, intensity modulated radiation and proton beam therapy - the most conformal form of radiotherapy possible. This is due to the high precision with which the seeds can be placed within the prostate gland, as well as the relatively low energy of the radioisotopes used. No other form of radiation therapy has been better able to localise a high radiation dose within the prostate while minimising the dose outside the gland.

1.2.6.3 High – dose rate brachytherapy

Another form of brachytherapy that has been used to treat prostate cancer is high-dose rate (HDR) brachytherapy. A limited number of centres in the U.S. use this technique, which employs high activity Iridium-192 (369 keV average), usually in combination with a course of external beam radiation. A robot assists in moving the radioactive sources through plastic catheters inserted in the prostate. As the radioactive source is removed from the patient at the end of each HDR treatment, the procedure is termed temporary brachytherapy. It is not possible to deliver an adequate radiation dose in a single session, and several administrations are required. The technique is associated with several problems, such as difficulty achieving optimal catheter stabilisation and faultless movement of the sources through the prostate. Because of these concerns, combined with the lack of long-term outcome results with HDR brachytherapy treatment in prostate cancer, some institutions do not employ temporary implants at this time and they use permanent implants with I-125 or Pd-103 [2,20]. Some models of the seeds are shown in Fig. (1.2.2.) [21,6].

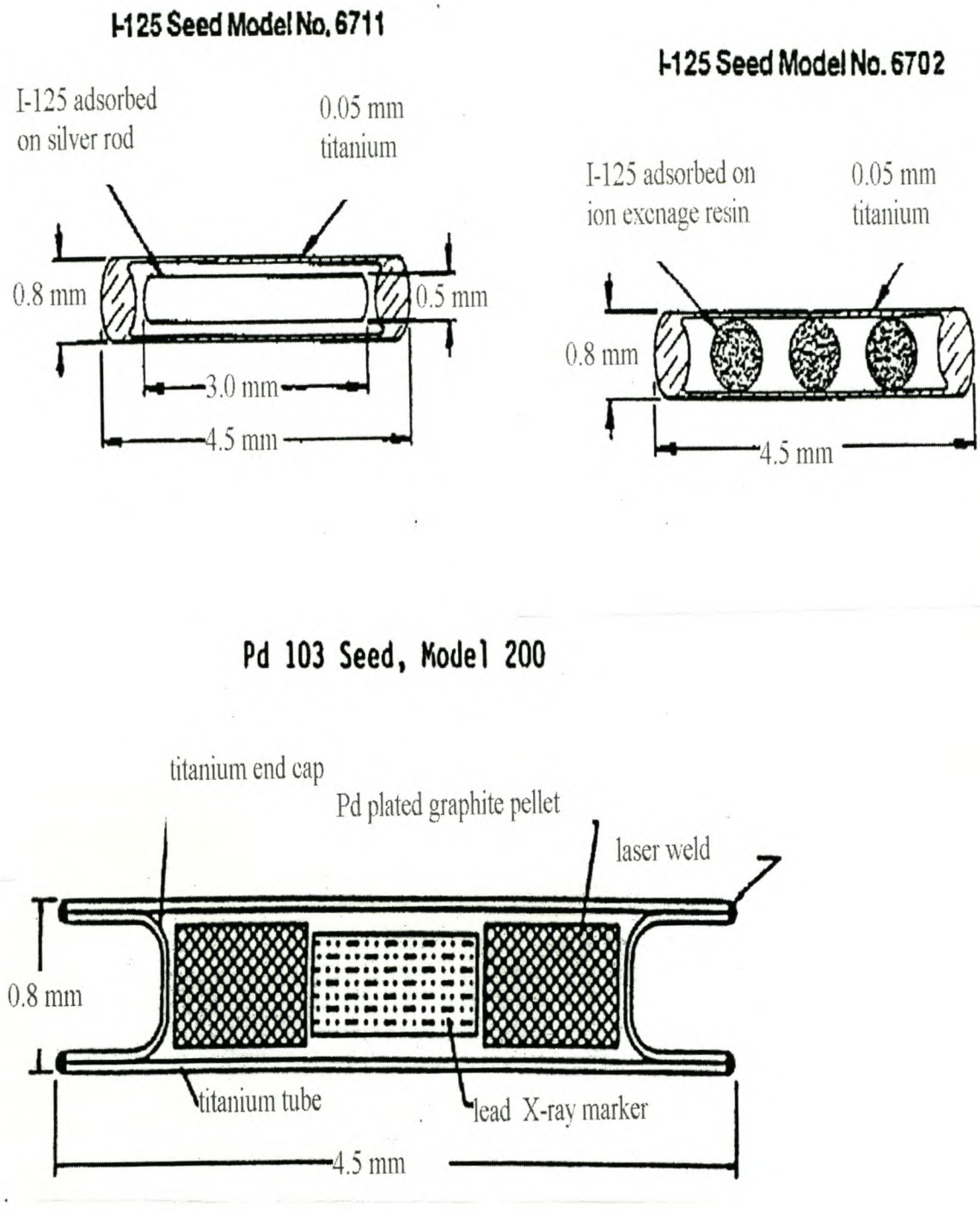

Fig.1.2.2. I-125 and Pd-103 seeds characteristics

1.2.6.4 A three - step process

Modern prostate brachytherapy consists of a three-step process [21,2]: Treatment planning, operative seed insertion, and a post-procedure evaluation of the implant to verify that the radiation dose delivered was optimal. Both the preliminary work-up and postoperative evaluations can be done in the physician's office.

The primary purpose of implant planning is to assure a systematic approach to the individual patient, wherein a thorough evaluation of prognostic variables, morbidity factors and patient preferences all play a part in determining what would be the most suitable therapy. The treatment plan has three components: patient selection, isotope selection and seed mapping.

(a) Patient Selection

Patients selected for seed implant alone, as for radical surgery, must have strong clinical evidence of organ-confined disease. Although no generally accepted criteria for determining organ-confinement exist, increasing evidence suggests that clinical stage, Gleason score, and serum prostate specific antigen (PSA) assembled into predictive algorithms, may be helpful in identifying patients at risk for extra-prostatic disease.

In general, seeds alone are recommended for patients with biopsy Gleason scores less than 7, pre-treatment PSA values less than or equal to 10 ng/ml and non-palpable or small solitary lesions less than 2 cm in largest dimension. For patients with Gleason scores of 7 or greater, pre-treatment PSA values over 10 ng/ml and/or nodules greater than 2 cm in size, the risk of extra-prostatic disease increases. For such patients a combination of external beam radiation and radioactive seed implantation is frequently recommended. Other factors such as patient age, the number of positive biopsy cores, amount of tumour in each core, as well as the presence or absence of perineural invasion may also play a role in treatment selection.

For patients with several high-risk factors, neoadjuvant/adjuvant androgen ablation therapy may be added to reduce glandular volume, particularly when the ultrasound

images show a moderate amount of pubic arch overlaying the gland, which will interfere with needle insertion. Patients considered at risk for post-implant urinary retention may also be placed on a three-month course of androgen deprivation prior to placement of the implant. Patient selection factors are listed in Table 1.1.

Table 1.1: Selecting Therapy According to Patient Factors

	Monotherapy	Combination Therapy
Nodule	None or small	Large or Multiple
Gleason Score	2 –6	7 – 10
PSA	[is less than or equal to] 10 ng/ml	> 10 ng/ml
Biopsy	Unilateral Disease or Locally	Bilateral Disease or Extensive
Prostate Volume	< 60 ml	< 60 ml
Urinary Flow Rate	> 15 ml/sec	> 15 ml/sec

(b) Isotope Selection

Permanent implants, used as monotherapy or in combination with external beam radiation, employ one of two established low-energy radiation sources, namely, Iodine-125 and Palladium-103. Both are sealed within minute biocompatible titanium

cylinders. The titanium cylinders remain permanently in the prostate while the radioactivity decays to an inert state over several months. The main difference between the two isotopes is half-life, the time required for a 50% reduction in the radiation dose. The half-life, in turn, affects the initial dose rate of the implants: I-125, with a half-life of 60 days, emits radiation at 8 to 100 mGy (1 Gy = 1 J/ Kg) per hour at the time of the actual implant. Pd-103, with a half-life of 17 days, starts out at 200 to 240 mGy per hour. Based on animal models and radiobiological principles, Pd-103 is recommended for higher grade (Gleason score, greater than 6) tumours.

(c) Seed Mapping

For the volume study, patients are placed on the exam table in the dorsal lithotomy position. The body halves should appear symmetrical when bisected in the mid-sagittal plane. Attention to detail is important so that the individual patient's positions are readily reproduced in the operation room. The ultrasound probe, when inserted into the rectum should be perpendicular to the perineum, and the prostate gland images should be centred within the template outline of the monitor without compressing or distorting the gland. It then becomes a straightforward process to reproduce a similar arrangement in the operation room. Dose calculation can be best performed in an inexpensive office setting rather than intraoperatively with the patient under anaesthesia.

During the transrectal ultrasound volume study, a series of cross-sectional images of the prostate gland are obtained at 5-mm intervals from apex to base, including the seminal vesicles. These cross-sectional ultrasound images are entered into a treatment-planning computer to be digitised and reassembled into a three-dimensional rendition of the gland that corresponds to its true anatomical structure. The radiation oncologist determines the number of seeds, seed activity, and their placements within the prostate in compliance with the prescribed total dose. The treatment planning system is interactive, allowing the radiation oncologist to observe resultant changes in isodose distribution that occur with changes in seed positioning.

Intraoperative Seed Placement: The entire seed implant procedure generally takes 45 to 60 minutes, and the total patient stay in the ambulatory surgery centre about 3

hours. The patient is anaesthetised and placed in the dorsal lithotomy position, duplicating the office volume-study position. The ultrasound probe with its attached template is inserted into the rectum at a 10-degree downward angle to the operating table to align the long axis of the probe with the slightly downward direction of the rectum. The probe is adjusted so that the cross-sectional images correlate with the pre-plan volume study images. Once the probe is in the appropriate position, it is locked to the operating table by a stabilising device. The probe rests in a "stepper", which permits precise forward and backward movements of the transducer in 5-mm increments, providing sonographic images of the gland from its base to apex. It also provides sagittal views of the prostate to assure correct depth placement of the implant needles.

The prostate is a very mobile and malleable organ and real-time monitoring of the needle insertion is of utmost importance. Any deviation and internal distortion should be recognised and corrected for. At the end of the procedure, the overall implant quality is evaluated by both ultrasound and fluoroscopy, and additional seeds may be placed as deemed necessary. Patients leave the operation room with an indwelling Foley catheter in the bladder, which is removed when the anaesthesia wears off.

Upon discharge from the outpatient facility, most patients resume their customary daily activities within a day or two. Postoperative medications generally include an antibiotic, a nonsteroidal anti-inflammatory agent, and an alpha-blocker.

Evaluation of implant quality: Implant quality is assessed using a three-dimensional reconstruction of the implant based on computed tomographic (CT) images obtained within 16 hours of the implant. The CT images document seed positions in relation to the prostate and adjacent structures, which permits computation of the aggregate dose meted out to both the prostate and surrounding structures. The CT-defined images are overlaid with isodose curves and a DVH constructed to verify adequacy of treatment and compliance with the planned implant.

Post-implant follow-up: Patients are generally evaluated every three to six months the first year, and annually thereafter. The follow-up includes clinical evaluation and

serum PSA measurement. The necessity for additional studies is dictated by patients' symptoms and signs [22,2].

1.2.6.5 Outcome evaluation and definitions

The American Society for Therapeutic Radiology and Oncology (ASTRO), defines biochemical (PSA) failure as three consecutive PSA increases measured six months apart. In addition, it is also considered a local failure when a positive needle biopsy is taken 18 months or more post-implant, while a positive bone/CT scan is considered as distal failure.

1.2.6.6 Results with prostate brachytherapy

At Northwest Hospital, 229 patients with stage T1/T3, low to high Gleason grade prostate cancer underwent prostate implants with I-125 or Pd-103 between January 1, 1987 and September 1, 1989. In this study patients, whose median age was 70 years (range 53 to 92 years), were divided into two groups based exclusively on clinical stage and Gleason grade. Pre-treatment PSA measurement was obtained in all patients but did not impact upon the treatment group assignment.

Group 1 consisted of 147 lower stage/grade patients treated with an implant alone (monotherapy) and Group 2 comprised of 82 patients deemed to have higher risk of extra-prostatic extension of the malignancy. Group 2 patients, in addition to receiving a seed implant, were also treated with 45 Gy external beam radiation to the pelvis (combination therapy). None of the patients underwent operative staging and none received concurrent androgen manipulation.

Fourteen patients were lost to follow-up: seven by death from non-cancer causes within 18 months post-implant and seven because of incomplete PSA follow-up, leaving 215 patients for complete evaluation. The median duration of post-treatment follow-up was 110 months.

The observed disease-free survivals of the two groups combined at 12 years was 70%; 66% in the monotherapy group and 79% in the combination therapy group [2].

Treatment-Related Morbidity

Studies on more than 4,000 patients treated show that most implant patients experience some degree of irritative and/or obstructive urinary tract symptoms lasting for a couple of weeks to months [2]. The symptoms are generally mild, but may be a bother to patients who expect rapid recovery and to return to pre-implant health.

Urinary retention requiring intermittent or long-term catheterization is uncommon, occurring in fewer than 5% of brachytherrapy patients. It has been noted that a subset of patients presenting with enlarged glands and pre-existing urinary obstructive symptoms are particularly prone to develop acute retention. It has been experienced that urinary obstructive symptoms immediately after seed implantation are caused primarily by the mechanical trauma of the implantation rather than from the radiation. Radiation-induced symptoms may appear similar, but generally do not appear until several days after the implant. Symptoms generally peak after about seven to 10 days after Pd-103 implants and 14 to 21 days after an I-125 implant. Large glands which require greater numbers of seeds, may be subjected to more trauma from needle punctures than smaller glands.

The risk of impotence increases with age and averages 30% for all ages. It has been shown that post-implant erectile dysfunction may be largely related to age and degree of pre-treatment erectile competence. Patients younger than 60 years of age, who claimed sexual fitness prior to the implant, generally maintained their sexual competence postoperatively; in contrast, about 20% of patients between 60 and 70 years of age who claimed to be sexually active before the implant suffered erectile dysfunction after the procedure. The sexual dysfunction rate appeared similar for patients treated with seeds alone and with combination therapy. Likewise, it has been discovered that patients without a prior transurethral prostate resection (TURP) have little or no risk of becoming incontinent of urine. In patients with a TURP history, however, the incontinence rate is 24%. This led to modify the implant technique by shifting some of the central seeds away from the urethra in TURP patients, which appears to have largely eliminated this unfortunate side effect [2,15,18].

1.3 AN INTRODUCTION TO NUCLEAR REACTION AND RADIONUCLIDE PRODUCTION

1.3.1 Nuclear reactions

The unstable nuclides are obtained by bombarding the stable nuclides with beams of particles, which are produced either in accelerators or in nuclear reactors. The accelerator represents one of the fastest growing instruments in our age of technology growth. Over the last 50 years the energies which can be produced in the accelerators have increased by a factor of one million, and the types of particles which are being accelerated have enormously diversified. In the beginning only ions of the isotopes of the two lightest elements (hydrogen and helium) were used, while now any element, usually multiply ionized, can be accelerated [23].

The radioactive isotopes can be produced with most accelerators presently available and every kind of particle beam. As the energy of the particle beam increases, more neutrons can be expelled from a given stable nucleus and a number of neutron deficient radionuclides are obtained which need several beta decays before returning to the stability line. The fact that one obtains several radionuclides, instead of the one needed, and that in most cases a series of decays are in course, usually do not represent desirable features for radionuclide use. If one adds a highly increased cost factor, it is understandable why the production of radionuclides for medical use is confined to lower energy accelerators, mainly cyclotrons, accelerating alpha-particle, deuterium, and proton beams to energies below 30 MeV.

The radionuclides produced by accelerated charged particles are complementary to those produced by neutrons in the nuclear reactors. When a neutron is added to a nucleus, it usually transforms one of its neutrons into proton expelling a negative beta particle. On the other hand, when a charged particle from the accelerator enters a nucleus, a proton is usually transformed into a neutron and either a positron is emitted, or electron capture takes place, in which photons carry away most of the decay energy. Generally, the reactor-produced radioactive nuclides are mostly used

when local ionization by electrons is of interest, while cyclotron-produced radioisotopes are useful for obtaining photon signals about the localization of radioactive nuclide.

1.3.1.1 Processes in the target

When a beam of charged particles bombards a target, several processes can occur:

1. Beam particles collide with atomic electrons producing *ionizations* and *excitations* of atoms and molecules in the target. The energy of the beam particles thereby decreases, while the part of energy transferred to the target dissipates finally into heat.
2. The probability of collision with relatively very small nuclei is much smaller than compared to the collision with electrons. If the particle does not come into a close interaction with the nucleus an elastic nuclear collision might take place, in which a part of particle's kinetic energy is transferred to the nucleus, setting it in motion as a whole. Most of the energy of the moving atom is also dissipated as heat. The internal state of the nucleus remains unchanged.
3. A still closer interaction with the nucleus may produce internal disturbances, in a way similar to those taking place in the electron cloud (excitations and ionizations). The energy received from the bombarding particle may be used for excitation of the nucleus. This is called inelastic nuclear scattering. The de-excitation takes place usually in a very short period, with the emission of one or more gamma rays.
4. Another possibility is that the bombarding particle is absorbed by the nucleus, with the result that its released binding energy brings the nucleus into a highly excited state. The de-excitation can take place in two ways: (1) several gamma rays may carry off the excitation energy. The final result is that the incoming particle is captured and a new nucleus is formed, which is radioactive. The most interesting case, for the radionuclide production is the neutron capture, which is symbolically shown as (n,γ); (2) the excitation energy of the nucleus may be concentrated on one or more of its constituents, which can then leave the nucleus. If alpha-particles are accelerated, they can expel, in simplest cases, a proton or a neutron or two neutrons, which is symbolically shown by (α,p), (α,n) or $(\alpha,2n)$.

As a rule, in these cases also, a radioactive nucleus is produced. A general name, for both alternatives is a *nuclear reaction* [23].

To summarize, there are three limitations regarding the radionuclide production:

1. Target heating. Much of the beam energy is spent in heating the target. Efficient cooling is necessary and the dimensions of the target are also limited.

2. Beam energy loss. Since the nuclear processes are usually very sensitive to energy one can choose the best beam energy, but as the beam penetrates through the target its energy is rapidly decreasing. One has to integrate over an energy interval.

3. "Impurities". More than one reaction is often possible with a single nuclide, the probabilities being very different. Very often, the irradiated element consists of several stable nuclides, so that the number of produced radioactive nuclides is proportionally increased. The target may also contain various kinds of impurities due to the preparation process and environment. After irradiation the target would contain, as a rule, several radioactive nuclides.

1.3.1.2 Reaction cross–sections

The design and interpretation of a nuclear reaction experiment requires three different kinds of information:

1. Initial physical and geometrical conditions. First, we should know quantitively what are the particles in the beam, their mean energy and energy spread, and the geometry of the beam. Next, we should know the chemical composition of the target, its physical characteristics and its geometry. Finally, we should know what happened during the experiment to the parameters that could vary, such as the beam intensity and energy.

2. The results of experimental measurments. We usually have to establish at least one of the following parameters: intensity, energy, type of particles or systems, and the angles of emission, if it is taking place.

3. Laws and models. When preparing the experiment one always knows, more or less, the physical laws governing the processes, which one expects that should take place. The degree and the precision of one's knowledge might vary a lot, but one should know all that is needed in a radionuclide producing reaction. One's knowledge might be just at the level of empirical law, or at higher degree of a theoretical mode, or finally, one might possess an adequate theory.

The most important question for interpretation may be reduced to what happens when one particle of the beam interacts with one system of the target, a nucleus, or an atom. What one knows about it is expressed in the probability for a given process, which we denote by σ. Since in nuclear processes we are mostly interested in nuclear forces which are confined to nuclei, a nuclear reaction is taking place mainly when the particle enters the nucleus. Geometrically, an incoming particle "sees" the cross-section of the nucleus, and the larger the cross-section the more probable is their interaction. For that reason, the probability of interaction of one particle with one target system is called cross-section σ, has the dimensions of a surface and a unit is chosen approximately equal to the cross-section of a nucleus, which is 1 barn = 10^{-28} m^2 [23].

The cross-section σ contains the information from our third set – the laws and models. Their numerical values are obtained by using some information from the first set: what are the particles, their initial energies and the initial geometry. When the determination of σ is completed, we continue with information from the first set which are needed to pass from the interaction of one particle with one target system, to the interaction of a beam with macroscopic target.

Suppose that there are N_0 target systems per unit area, and that their number is relatively so small that an incoming particle can see them all, none of them being hidden behind the system. Then, the probability that one particle per unit area and unit time shall interact with N_0 systems per unit area is equal to N_0. If the beam contains I particles per unit area and unit time, the number of interactions dI is given by

$$dI = I\sigma N_0 \qquad (1)$$

Three-dimentional clarifications should be added. The number of targets per unit area N_0 is equal to the number of atoms per unit volume, multiplied by the thickness of the target. The number of atoms per unit volume can be expressed by density, atomic mass and Avogadro's number. Care should be taken to differentiate between the old and new units. Equation 1 is valid for the density of the beam per unit surface. In

order to get the total number of interactions, a multiplication by the cross-section of the beam is needed.

We have supposed that the target is thin, so that the beam sees all the atoms. The incoming particle does not produce a nuclear reaction with every nucleus that it sees. The thinness of the target depends on σ.

1.3.1.3 Excitation curve (Excitation function)

A nuclear reaction, like any other process in nature, depends on the energy in a selective way. A curve showing how the probability of occurrence of a nuclear reaction depends upon the energy of the bombarding particle is called excitation curve or function. It represents the cross-section for a given reaction as a function of the energy of the incident particle. Since often more than one reaction is possible, especially at higher bombarding energies, the excitation curves permit the calculation of relative reaction yields for a given energy interval. Figure 1.3.1 illustrates excitation curves for the production of ^{103}Pd from ^{nat}Ag [8] in a 66 MeV cyclotron. In addition, the target element very often consists of several stable isotopes, also giving rise to the production of several radioisotopes even if only one type of nuclear reaction is energetically possible [23].

Radioisotopes having the same Z as that of the desired radioisotope, of course, are of the same element and they can, therefore, not be chemically separated. Minimizing the radiocontaminants of this kind can be achieved by a careful choice of the bombardment parameters, such as the type of bombarding particle, target material and the energy range in which the radioisotope is to be produced. In developing a suitable production route for a medical radioisotope, it is crucial not only to know the excitation functions for the various possible production routes, but also those for the production of the other radioisotopes which will eventually end up as radiocontaminants in the final product in each case [24].

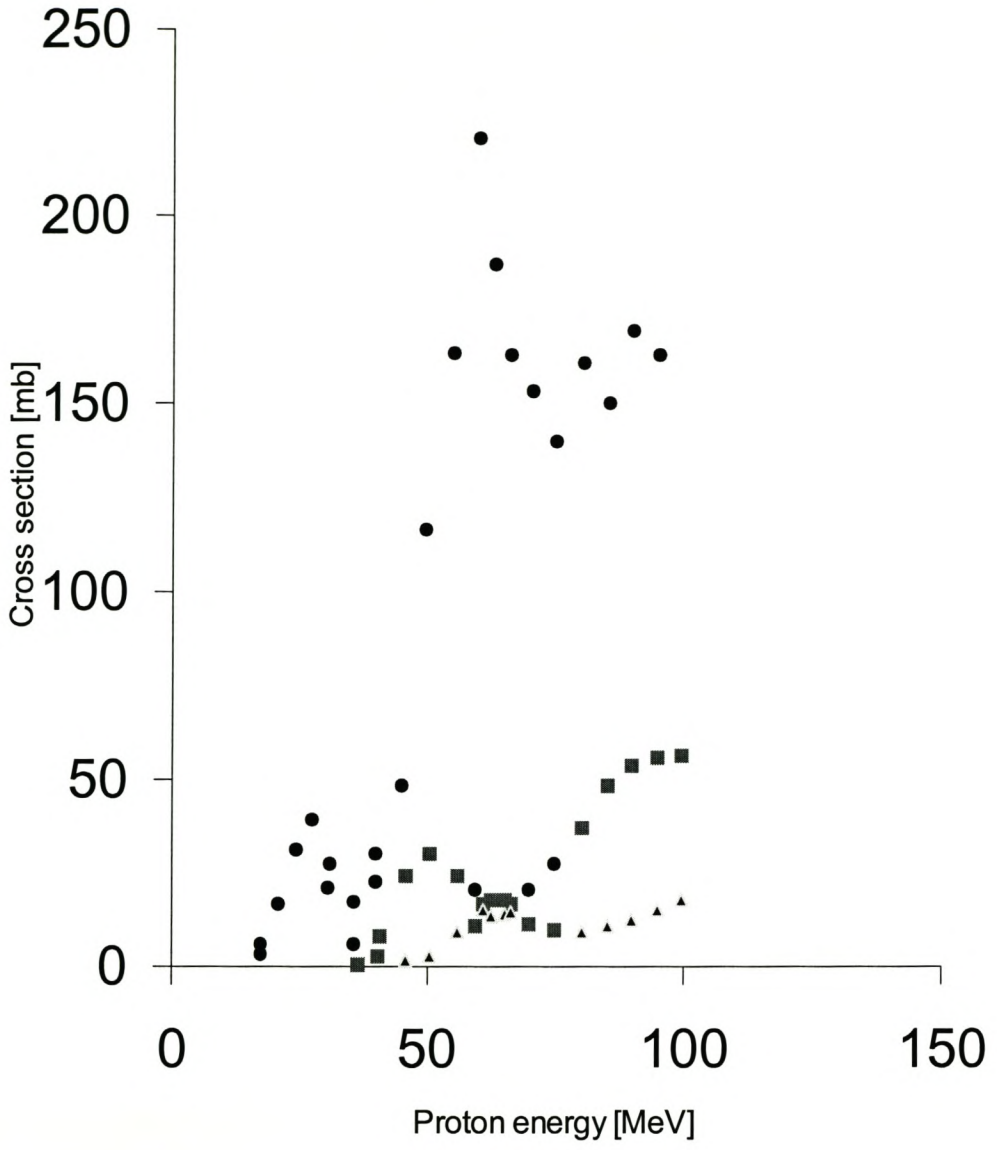

Fig.1.3.1. Effective cross sections for the processes $^{nat}Ag(p,xn)^{103}Pd$ (•), $^{nat}Ag(p,xn)^{101}Pd$ (■) and $^{nat}Ag(p,xn)^{100}Pd$ (▲).

Nuclear reaction cross sections can be calculated by using one of a variety of computer codes available. The code ALICE [24] has been specifically recommended for use by non-nuclear physicists for the calculation of excitation functions, therefore,

when calculations of this nature are required in the field of radioisotope production, preference is often given to the use of ALICE. This is also one of the main computer codes currently being evaluated in a long-range benchmark intercomparison of medium energy cross-section codes and it was recommended to be included in an intercomparison of codes suitable to be used for predicting unknown cross-sections in the field of medical radioisotope production.

Generally, the calculated excitation functions are in agreement with the experimental data. In general, therefore, the theory is regarded to be capable of the incident energy ranges required for the optimum production of a particular radioisotope under various bombardment conditions.

For production purposes, usually, it is desirable to have production-rate curve, or *yield*, as a function of incident particle energy, which is derived by integration of the experimental excitation function. Usually, the yield is obtained at the *end of bombardment* (EOB) and this practical yield can be compared with the theoretical one [24]. Figure (1.3.2) shows the excitation curve together with practical yields for the production of ^{103}Pd from Rh targets [25]. For a routine production, yield is very helpful because sometimes after separation chemistry we find that the activity is less than what expected from the yield and we have to look for the problem either in the chemistry process or in bombardment station or both.

There are a few computer programs which are used for the calculation of thin and thick target yields (in which particle beam is stopped) [24].

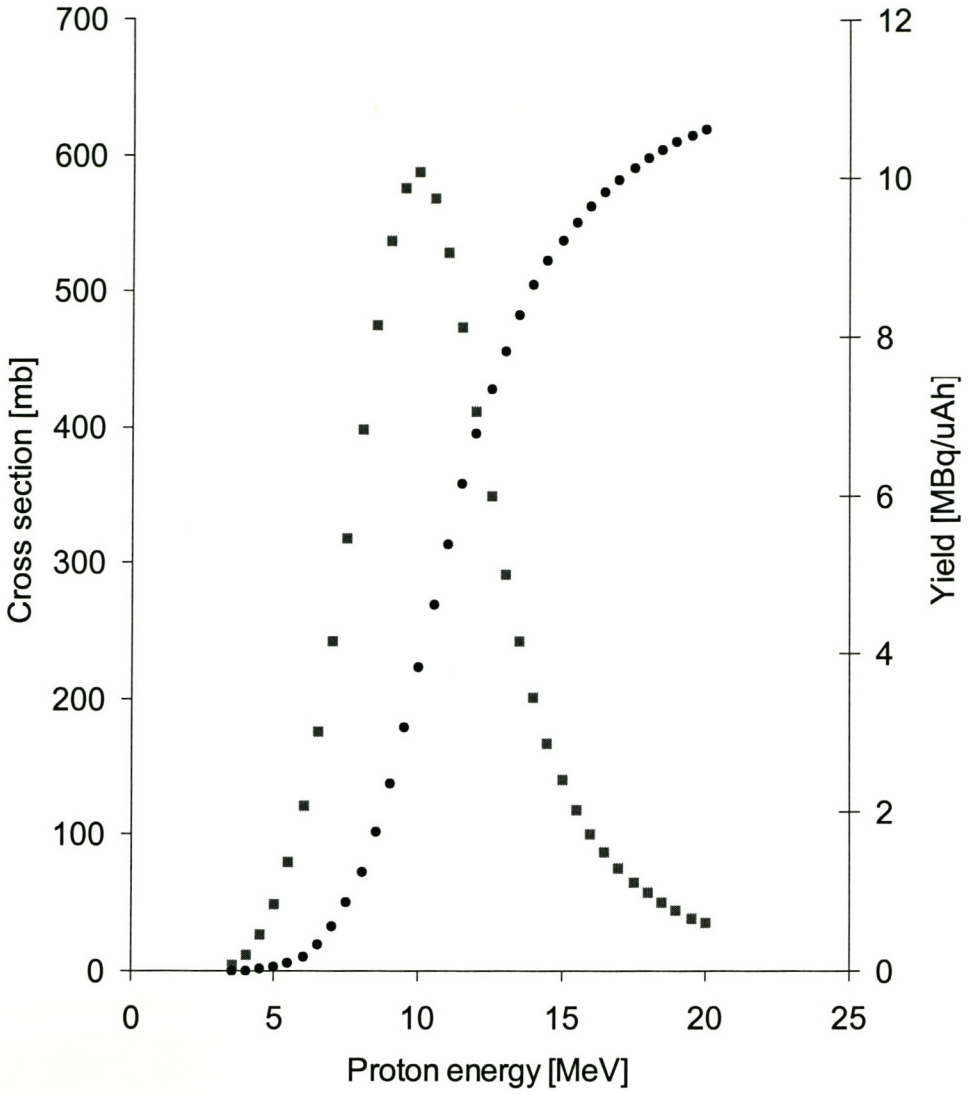

Fig.1.3.2. Excitation curve for the ^{103}Rh(p,n) ^{103}Pd reaction (■) and derived thick target yields (•).

1.3.1.4 Reaction mechanism and their relation to excitation functions

Different processes can take place when a proton, for example, induces a nuclear reaction in a target nucleus. The mechanisms involved in nuclear reactions have been treated by means of many different models. In general, one can distinguish between two extreme reaction mechanisms *viz.* compound-nucleus reactions and direct reactions. In compound-nucleus reactions the proton is absorbed in the target nucleus. The resulting compound nucleus then attains statistical equilibrium, due to the sharing and re-sharing of the proton energy among the nucleons without particle emission. Within a very short time (10^{-16}–10^{-18} s), the excited compound nucleus decays by emitting particles and γ-rays until it finally reaches the ground state. By contrast, direct reactions take place immediately (within ~10^{-22}s) without passing through the compound-nucleus stage. Such a reaction involves a single interaction between the proton and one or several nucleons. In addition to these two mechanisms, experiments have shown the existence of pre-equilibrium reactions which, in terms of duration and complexity, lie between compound-nucleus reactions and direct reactions. In general, the particles emitted during pre-equilibrium emerge with considerably higher energies than those evaporated from a compound nucleus.

For a given nuclear reaction, all three mechanisms generally contribute to some extent. The compound-nucleus cross-section of a particular reaction usually rises rather rapidly immediately above its threshold energy, reaches a maximum at a few MeV above threshold and then falls due to competition from other reactions as their thresholds are also surpassed. Whereas the peak region of an excitation function is representative of compound-nuclear processes, the tail region is determined mainly by pre-equilibrium processes [24].

1.3.1.5 Residual Radioactivity

Many of the residual nuclei produced via nuclear reactions are unstable and they subsequently decay via one or more of the radioactive decay modes (α, β or γ decay) in order to return to stability. Large numbers of radioactive nuclides are, therefore, produced in the bombardment of target material with charged particle beams,

resulting in high levels of residual radioactivity. Mainly neutron-deficient radioisotopes, which principally decay by means of the emission of positrons (accompanied with annihilation γ-rays and, in most cases, also with other γ-rays), are produced in this way. The residual radioactivity induced in a radioisotope production target usually results in the emission of a complex mixture of radiation and sufficient steps must be taken to prevent the over-exposure of personnel [24].

1.3.1.6 Neutron Radiation

Neutrons, being one of the primary particle types ejected in a nuclear reaction, are produced in great numbers when a radioisotope production target is bombarded by a proton beam. Other particles, such as protons, alpha particles, etc. are also produced but they are rapidly slowed down and stopped in or close to the target. Unlike charged particles, neutrons experience no gradual slowing down when passing through matter. They interact only with nuclei and, therefore, travel great distances in material. As a result, they cause numerous secondary nuclear reactions not only in the material close to the target, but also in the walls of the room in which the bombardment is performed. A total yield of 9×10^{13} neutrons per second can be expected when a 100 μA beam of 100 MeV protons is stopped in a copper target. In general, their energies range from close to that of the incident protons down to the thermal region, the fast neutrons being emitted mainly in the forward direction and the slower ones isotropically. These neutrons are the main source of undesirable secondary activation of materials near the irradiated target and a major cause of radiation damage to sensitive components [24].

1.3.1.7 Beam loss due to non-elastic nuclear interactions

Although relatively small in most cases, the total non-elastic nuclear-interaction probability of an incident charged particle on a thick target is obviously not zero. Particles undergoing such interactions with the target nuclei are removed from the incident beam, which means that the particle flux is progressively reduced with depth as the beam penetrates the target. This effect is not very pronounced at low incident energies, such as 30 MeV,but rapidly becomes significant at higher incident energies.

Since the beam intensity reduces gradually as the particles penetrate the target material, the effect of the beam attenuation is, of course, felt more and more towards the end of the proton range, hence, very little effect on total thick-target production rates is expected in the case of 66 MeV proton beams. At higher incident energies, however, the beam attenuation becomes significant when the particles still have relatively high energies (and large ranges). This leads to significantly reduced total production rates [24].

1.3.2 Effects related to beam energy

A charged-particle beam accelerated in a cyclotron always has a spread in particle energy, although normally very small. The mean energy of the particles in a cyclotron beam is therefore commonly referred to as the beam energy. Similarly, the mean range of the charged particles in a particular target material is then defined as the penetration depth of the beam (given in mm or g/cm^2). The energy spread ΔE in external beams used for radioisotope production is small compared to the beam energy E. For a typical 66 MeV proton beam ΔE (FWHM) <0.5 MeV [24].

1.3.2.1 Penetration depth

The penetration depth of charged particle beams and, therefore, the number of target atoms "seen" by the penetrating particles increase rapidly with increasing beam energy (see Fig.1.3.3). Since the number of nuclear reactions per unit time induced in a target by the particle beam is proportional to the number n of target atoms per unit area (see equation (1)), it follows that for a constant σ_i the nuclear reaction rate scales with the penetration depth of the beam. Higher-energy beams, therefore, offer greatly increased radioisotope yields but, on the other hand, one is faced with an equally increased neutron and γ-radiation problem. Not only are more particles produced per nuclear reaction, many are emitted with high energies. Radiation damage of sensitive components and secondary neutron-induced activation of the material in the irradiation vault, especially those in the immediate vicinity of the target, are greatly

increased. Another disadvantage is that more material is irradiated, and that the use of isotopically-enriched targets becomes very expensive.

One of the main advantages resulting from the greater penetration depth of higher-energy beams is the fact that it becomes possible to employ so-called tandem targets. In such a target more than one target material is stacked together and irradiated with the same beam. In this way, more than one radioisotope can be produced simultaneously [24].

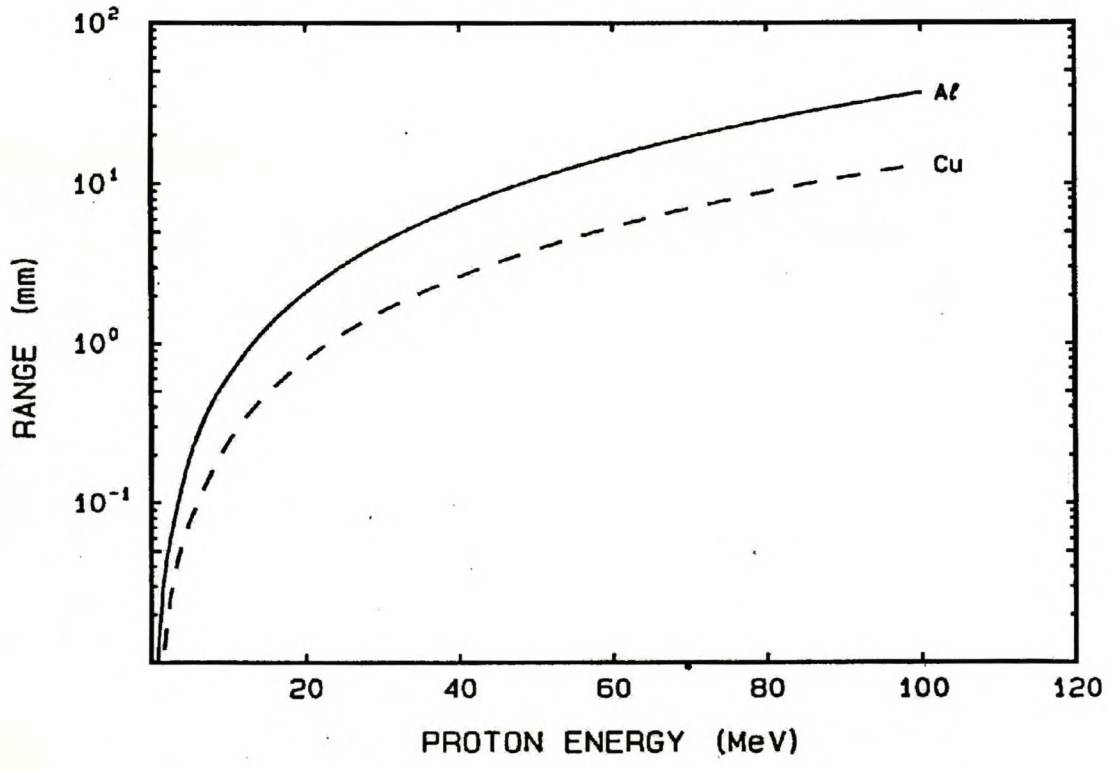

Fig.1.3.3. Proton range or penetration depth in solid Al and Cu as a function of proton energy.

1.3.2.2 Power dissipation

Since the beam is usually stopped in a radioisotope-production target assembly, the power dissipated in such an assembly is directly proportional to the product of the beam energy and its intensity. High-intensity beams therefore, in principle, aggravate the cooling problem. Since these beams have a greater penetration depth, however, it becomes physically possible to cool the target more efficiently. This is illustrated in Fig.1.3.4. At low energies the beam penetration is so small that the radioisotope production targets are usually cooled on the rear side only. At higher beam energies, the beam penetration increases and the introduction of a cooling water layer at the front surface becomes possible without a serious drop in primary beam energies. Even more cooling water layers may be introduced at still higher beam energies [24].

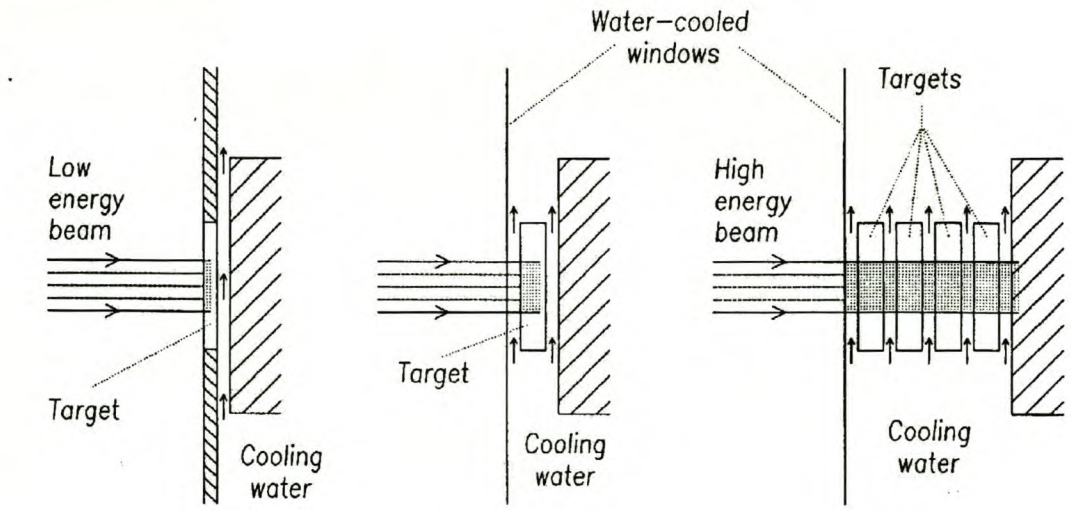

Fig.1.3.4. Illustration of different approaches to the cooling of radioisotope production targets.

1.3.3 Radionuclidic purity of a radioisotope

Radioisotopes for medical use are subject to the most stringent requirements on its chemical, radiochemical and radionuclidic purity (see also section 1.4, Chemistry). High radionuclidic purities are usually required in order to obtain high-quality SPECT images of the activity distribution and/or to minimize the radiation dose to the patient. Whereas chemical and radiochemical impurity levels in a product are determined solely by the efficiency of chemical procedures, its radionuclidic purity is determined by both chemical and physical considerations. Two types of radionuclidic impurities may be present in the product and it is important to distinguish between them. Radioisotopes of elements other than that of the desired product can usually be reduced to acceptable levels by exploiting chemical differences. Radioisotopes of the same elements as that of the product are, however, chemically indistinguishable from it. The levels of these radioisotopic impurities can be controlled only by changing parameters of the production route (e.g. nuclear reaction, particle energy, target thickness), by taking advantage of a difference in half-life (allowing shorter-lived radioisotopes to decay), or by actual physical isotope separation [24].

1.3.4 The importance of nuclear data

Nuclear data relevant to the production and application of radioisotopes can be divided into two groups, *viz.* decay data and nuclear cross-section data. In evaluating the suitability of a particular radioisotope for medical application, nuclear decay data are of prime importance. In general, these data are known with sufficient accuracy and various extensive compilations exist. Nuclear cross-section data, on the other hand, are of great significance in the production and radionuclidic quality control of radioisotopes. Knowledge of these data is important for calculating the expected yield of a particular radioisotope, as well as of the radioactive impurities expected to be produced via competing nuclear reactions. The ratios of the yield of the desired radioisotope to those of its radioisotopic impurities are of special concern. Doing such calculations for different production routes and energy intervals (target thicknesses) enables one to determine the optimum production route, incident

energy and target thickness for the production of a particular radioisotope for a particular use.

At low beam energies, where the number of competing nuclear reactions are small, the production of radionuclidic impurities usually does not occur, especially when an isotopically enriched target is used. Only the excitation function constructed from nuclear cross-section data relevant to a particular production route is in this case necessary to estimate the expected yield of the desired radioisotope. At higher beam energies, however, where a large number of competing nuclear reactions are possible, a wide variety of radionuclidic impurities are produced in addition to the desired radioisotope. This problem can become quite severe, especially when materials of natural isotopic composition are used as targets. Accurate excitation function data of all the relevant nuclear reactions are, therefore, required in order to minimise the level of radioisotopic impurities by carefully selecting a beam/target combination as well as an appropriate production energy window [24].

1.4 CHEMISTRY

1.4.1 Radiochemical processing of activated targets

The processing of activated targets involves the various aspects of purifying and isolating radionuclides after their production by a nuclear reaction. This aspect of radionuclide production is, of course, central to providing radionuclides for use in chemical, physical, biological, and medical studies. The selection or development of an appropriate processing method is affected by several, sometimes inter-related, factors. Nuclear and radiochemical considerations are largely determined by the nature of the target material, the activation process and the chemical identity of the product radionuclide. The chemical separation and isolation process is designed to permit recovery of the purified radionuclide in a form that is suitable for its intended application. Within the constraints imposed by the factors outlined above, the development of a suitable radiochemical processing method focuses upon: (a) separating the product radionuclide from the bulk target material; (b) removing unwanted traces of chemical and radionuclidic impurities; and (c) recovering the product radionuclide in a suitable chemical form and concentration [23].

It is useful to point out that, while newer, more efficient, more reliable, and faster procedures continue to be developed and to appear in the current literature, the older references still serve as useful sources of information on procedures and techniques, which can often be easily adapted to meet an immediate need. It is almost always simpler, easier, and more cost effective to modify an existing technique or method than it is to develop an entirely new one, although this is not always possible.

1.4.1.1 Nuclear and radiochemistry

The type and operating characteristics of available nuclear facilities place limits on the nuclear reactions which are possible choices for use in radionuclide production. These considerations restrict target choice and design, which in turn restricts the chemical approaches which will be suitable for processing. If accelerator production

is intended, the types of particle beam which are available, their energies and beam currents, are taken into account. In a reactor facility, the available thermal and fast neutron fluxes, both in steady-state and pulsed modes, are considered [23].

Fortunately, most of the time once the intended application is known and the mode of radionuclide production is chosen, a great deal of information in the form of literature references and other accounts of previous work is available. The methods and techniques, which are used for radiochemical processing of activated targets, are often surprisingly independent of the type of nuclear reaction used for radionuclide production. Rather, the processing methodologies focus on the chemical differences, or similarities, between the target and the product radionuclide or nuclides. Many of the processing schemes, which are now used for isolating accelerator-produced radionuclides, are directly derived from methods which were originally developed for reactor production applications. For example, the distillation methods which are used for the separation of ^{123}I from enriched ^{123}Te or ^{124}Te targets [22], represent modification of the procedures which were originally developed for the separation of neutron activation produced ^{131}I from a Te target. Likewise, many of the well-developed radiochemical processing methods for the transition metals, such as Cu from Zn, In from Cd, can be used equally well with accelerator or reactor-produced radionuclides. This applies even more so to processes developed for fission products or when the (n,p) or (n,α) routes for reactor production are involved.

Although the chemistry used in processing activated targets usually depends simply upon the nature of the target material and product radionuclide, one important difference between accelerator and reactor products is often encountered. In reactor production by thermal neutron activation, the (n,γ) process, the product radionuclide is isotopic with the target itself, since no net change in Z (the number of nuclear protons) occurs. Unless some special provision has been made to take advantage of the chemical effects of the nuclear transformation, the target material and product radionuclides are chemically indistinguishable. With accelerator processes, since a nett change in Z usually accompanies the nuclear reaction, the target and product represent different elements and are relatively easy to separate by conventional chemical means. Production and isolation of radionuclides at very high specific

activities are usually more easily achieved with accelerator production or as a result of fission if a reaction is used. Once again, exceptions are those nuclear reactions, which are induced by "fast" neutrons and result in non-isotopic products. The $^{32}S(n,p)\ ^{32}P$ reaction is an example of such nuclear production routes. A more complicated example takes place in fission of ^{235}U, which results in the production of one or more radioisotopes (in noticeable yields) of all the elements with Z between 65 and 167. To isolate and purify ^{99}Mo and ^{131}I, for example, these two radioisotopes have to be separated from all the other unwanted radioisotopes as well as the large quantities of uranium and aluminum originating from the target [24].

1.4.1.2 Radiochemical separations

Regardless of the mode of radionuclide production, the radiochemical processing scheme invariably consists essentially of one or more of the conventional chemical separation methods, such as distillation, extraction, precipitation, or chromatography, which has been adapted to satisfy the unique requirements which are imposed when large amounts of radioactivity are involved. The speed with which such separations must be performed depends most importantly upon the half-life of the product radionuclide. A great deal of effort has gone into the development of separation methods, which are suitable for use when ultrashort-lived radionuclides are to be processed.

A. Precipitation

Separations, which are based upon precipitation techniques, rely upon the different solubilities of the target and product radionuclide in a selected solvent system. While this type of purification step may be used at any stage of target processing, precipitation is most frequently used early to reduce the total mass of material which must be manipulated in subsequent operations. Most commonly the target material, which is present in the greatest mass, is precipitated out and removed by filtration or centrifugation while the product radionuclide remains in solution. When a sufficient mass of the radioactive element is present, or when a non-isotopic carrier has been added, the product radionuclide can be precipitated and removed from solution. While precipitation techniques are quite useful for removing the large mass of target

material from the small quantities of product radionuclide, the selectivity of such separations are often inadequate for achieving required chemical, radiochemical, and radionuclidic purity. In addition, the product radionuclide is often sorbed upon the surface, or included within the structure of the precipitate and substantial loss of radioactivity can result. This difficulty is usually most severe when very small masses of product radionuclide are involved, as is the case when high specific activity products are desired. For all of these reasons, simple precipitation alone is rarely adequate to provide a suitable processing scheme. Precipitation methods are also relatively difficult to perform in a hot-cell and require more sophisticated equipment [23].

B. Solvent extraction

Purification by solvent extraction is based upon the partitioning of solutes between two immiscible solvent phases. This technique has been one of the most widely used methods in the separation of target materials from product radionuclides. Solvent extraction is a relatively simple and rapid technique, which can achieve extreme selectivity. It can be used effectively over a wide range of radionuclide specific activities, and the scale of the process can be adjusted to accommodate widely varying masses of material.

Most frequently the distribution of solutes between aqueous and organic solvents are employed. A classical example of this approach is found in the extraction of elemental halogens into CCl_4 during the processing of radionuclides of Cl, Br, and I. In addition to this rather straightforward approach, the use of simple complexing ions, counter ions, chelating agents, and complexing or chelating organic solvents increases the versatility and position of solvents and temperature can also be manipulated to achieve satisfactory separations. Evaporation of volatile solvents or back extraction with an appropriate aqueous phase are commonly used methods for recovery of the product radionuclide [23].

Because solvent extraction is a relatively simple technique, it can be easily adapted as a remote or even automated operation. This is very attractive feature when large amounts of radioactivity must be processed repeatedly.

C. Chromatography

Chromatographic separation methods are closely related to the solvent extraction technique. In both cases, the separation depends upon the different distribution of solutes between two distinct phases. Since the phases move relative to one another during chromatography, a constant re-equilibration of the solute partitioning results. When viewed in this perspective, chromatographic separations can be thought of as a form of continuous, multiple extraction. For this reason, the previous brief description of solvent extraction is relevant to this discussion as well.

While essentially all types of chromatographic separations have been applied in one way or another to the processing of activated targets, liquid chromatography has been most frequently used. Systems based upon ion exchange, sorption, ligand exchange, reverse phase, etc. have been developed. The equipment used can vary from a simple burette, partially packed with ion exchange resin, to a complex, heavily shielded, remotely controlled, self-contained process assembly.

Perhaps the greatest attraction of chromatographic methods lies in the ability to achieve high resolution of closely related chemical species while, at the same time, minimizing direct manipulation of the equipment involved. For example, by proper selection of solvents, many of the transition metal radionuclides can be sequentially stripped off strong anion exchangers, since they form complex anions with the chloride ion. Subtle changes in solvent composition can dramatically affect the characteristics of such systems. Isolation of product radionuclides at high specific activities can be easily achieved, especially when the product is eluted first and tailing of unwanted impurities into the radionuclide fraction can be avoided. The limited capacity of chromatographic systems can often be expanded, by increasing column dimensions if necessary, although larger elution volumes must then be used. Column ion exchange chromatography has been regarded as the "state of the art" method by many analytical chemists [23]. For the reasons mentioned above, most of the next chapters are dedicated to ion exchange chromatography and ion exchange related chemistry of the elements involved in the production of ^{103}Pd; i.e. Pd, Rh, Ag, and Cu.

D. Volatilization

Radiochemical processing of activated targets by means of volatilization techniques, such as distillation or sublimation, can be used to advantage in a situation where the product radionuclide is a gaseous element, or when it can be readily converted to a volatile derivative. A variety of factors including the vapour pressures of constituents, their respective boiling points, and the physical nature of the target material affect the ease with which separations can be performed and the quality of the product obtained. In certain cases, very impressive separations can be achieved, and little additional processing of the product radionuclide may be required.

The volatility of Xe allows rapid and efficient separation of Xe radionuclides from molten salt targets. Technetium is readily isolated from MoO_3 by sublimation at elevated temperatures in a flowing O_2 stream [23]. As was previously mentioned, the distillation of I radionuclides from acidified aqueous solutions is a classical approach to processing activated Te targets. The production of ^{11}C as CO or CO_2 by proton or deuteron bombardment of B_2O_3 targets relies upon the convenient recovery of the gaseous products by the use of a sweep gas stream. In cases such as these, if high-specific activity products are being processed where small masses of product material are involved, special care must be taken when using a flowing gas stream to carry over the volatile product, otherwise, entrainment of unwanted chemical and radionuclidic impurities in the sweep gas may compromise the purity of the final product [23].

1.4.1.3 Quality control

What is possible in terms of radionuclide production is limited by the availability of physical facilities. What is appropriate in terms of nuclear reactions and radiochemical processing is almost invariably determined by the intended application. The acceptable levels of radionuclidic, radiochemical and chemical impurities are limited by consideration of the anticipated use. In addition, the required chemical form, concentration and specific activity of the product are restricted by this factor. Radionuclides are used in many applications, the details of which are beyond this discussion. In one primary use, however, as labelled compounds in biological and

medical studies, the most stringent limits upon acceptable radionuclidic, radiochemical and chemical purity are encountered [23].

A. Radionuclidic purity

The radionuclidic purity of a sample is defined as the fraction of the overall disintegration rate, which results from decay of the specified radionuclide, thus, if a radionuclidic purity of 98% ^{67}Ga and 2% ^{66}Ga is specified, 98% of the decay rate of the sample will be due to ^{67}Ga, while 2% results from decay of ^{66}Ga. Radionuclidic purity is usually measured by using a calibrated solid state counting system coupled to a multichannel analyzer for gamma ray spectroscopy. Detection efficiencies are determined by counting absolute radioactivity standards at a fixed geometry. Radionuclidic purity is calculated by comparing measured photon energies, abundances, and half-lives from the sample with those of published references. Absolute disintegration rates for the various radionuclides, which are present in the sample, are then derived [23].

Two types of radionuclidic impurities may be present in the product and it is important to distinguish between them. Radionuclides of elements other than the desired product can usually be reduced to acceptable levels by exploiting chemical differences during development of an appropriate processing scheme. Radionuclides that are isotopic with the product are another matter. Since they are chemically indistinguishable from the product, the levels of these isotopic radionuclidic impurities can be manipulated only by a modification of the nuclear parameters of production or by taking advantage of a difference in half-life and allowing shorter-lived isotopic radionuclides to decay.

High radionuclidic purity is required for products intended for use in almost all biomedical tracer applications. While the specific requirements may vary, consideration of this feature can be quite important. For example, if one wishes to study renal function in animals using ^{123}I-labeled o-iodohippuric acid and collimated probe detectors, high radionuclidic purity is required so that only the radioactivity in the detector field of view is registered. Scattered radiation from higher energy impurities, such as ^{124}I, are a potential source of interference in such a study. When

imaging studies in humans are used to assess renal function, even higher radionuclidic purity ^{123}I-labeled o–iodohippuric acid is required in order to assure the best image resolution, although the patient radiation dose may not be a major consideration because of the short biological half-life of o–iodohippuric acid. In studies using radioiodinated agents with relatively long biological half-lives, such as thyroid or adrenal studies, limits on radionuclidic purity are very high, both in order to obtain high quality images of the distribution of the label and also to minimize radiation dose to the patient.

B. Radiochemical purity

Radiochemical purity refers to the chemical identity of the specified radionuclide. For example, if 98% of the ^{99m}Tc in a certain preparation is in the form of ^{99m}Tc-DTPA, the radiochemical purity of the sample is said to be 98%, with a radiochemical impurity level of 2%. Radiochemical purity is usually measured by some adaptation of standard analytical technique. While the ease of detecting the activity in the various chemical forms once they have been separated into individual fractions simplifies such determinations, the possibility of altering the composition of high-specific activity preparations during an analysis is a constant concern, and many artifacts associated with such determinations have been described [23].

The need for high radiochemical purity in tracer applications is obvious. Assuming the absence of nonisotopic radionuclide impurities, relatively modest radionuclidic purity may be acceptable if only well counting or simple probe studies are contemplated. On the other hand, the use of a tracer is severely compromised if a significant fraction of the radioactivity is present in an inappropriate chemical form [23].

This can be of particular concern during the processing of radionuclides, which are intended for subsequent use in labeling. For example, in the production of F_2 for use in the synthesis of ^{18}F labelled organic compounds, a large fraction of the ^{18}F activity recovered from the target is sometimes found to be in chemical forms other than F_2. Moisture in the systems results in the formation of ^{18}F labeled HF, while the presence of N_2 and CO_2 in the target gas result in the formation of appreciable quantities of ^{18}F

labeled NF_3 and CF_4, respectively. The result is that, in cases where large amounts of radiochemical impurities arise, inadequate amounts of ^{18}F labeled F_2 are available for the intended use. In this case, careful attention to detail in conditioning of the target system and in assuring high purity target gas is required. In the processing of radioiodine nuclides by distillation, the product is recovered in dilute NaOH. Unless great care is taken, or a reducing agent is added to the alkaline solution, the radioiodine is recovered as a mixture of iodide and idodate [23]. If the subsequent labeling procedure reequires iodide as the starting material, the presence of radioiodate will result in lowered radiochemical yields.

In general, there are two strategies for resolving problems of radiochemical purity: (a) the radiochemical impurity can be simply removed, or (b) the impurity can be converted into the desired chemical form. If small amounts of impurity are involved they can usually be separated from the product by the types of chemical separations which have been described previously. When a significant amount of the product radionuclide is found to be in the unwanted chemical form, it is often more economical to go through a chemical cycle which converts all of the product to the desired form.

C. Chemical purity

The chemical purity of radioactive products is a reflection of the chemical composition of the sample, with specific emphasis on the amounts of non-radioactive components. The requirements for chemical purity associated with radionuclide production are sometimes less clear than are those for radionuclidic or radiochemical purity [23]. Certainly in some applications, such as the sealed sources used as counting standards, the chemical composition of the product is of little concern. At the other extreme, in radiopharmaceutical preparations which are intended for human use, the most stringent limitations on chemical purity come into effect.

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In addition to high radionuclidic and radiochemical purity, radiopharmaceuticals require verification of chemical parameters such as pH, ionic strength, and freedom from toxic and pyrogenic substances, as well as freedom from bacterial contamination. While it may be possible to purify and sterilize the final labelled

product after preparation, some special consideration of the unique requirements imposed by this intended use is appropriate. For example, the production of ^{111}In via the ^{112}Cd(p,2n) ^{111}In reaction is frequently used and suitable radiochemical processing schemes have been developed. One must consider, however, that Cd is an extremely toxic element and careful quality control is required to assure that the amount of Cd in the final product solution is low enough for safe use in humans. An alternative approach is to use the ^{109}Ag(α,2n)^{111}In production reaction, in which case the presence of a trace amount of Ag, which is significantly less toxic than Cd, in the final product is of less concern.

Another example of the special need for high chemical purity in product radionuclide solutions can be found in the use of the weak chelating agent, 8-hydroxyquinoline, for the labeling of human and animal cells in vitro with ^{67}Ga or ^{111}In. The traces of transition metals which are present in laboratory reagents used during labeling, as well as those left over after radiochemical processing, can interfere with quantitative formation of the labeled chelate intermediate. In this situation, not only must the processing scheme used for the production of ^{67}Ga or ^{111}In give a product which is low in total transition metals, but care must be taken to ensure that the highest levels of chemical purity in reagents are maintained.

The amount of "carrier" (or stable isotopes) present in radiochemical products are of concern for other reasons as well. Very high specific activities may be required for certain applications, such as radioimmunoassays or other competitive binding studies. The use of carrier during processing is precluded in products intended for many such applications. In general, however, the addition of carrier can improve reliability and frequently simplifies the required processing chemistry, such as the addition of iodide during ^{123}I processing by distillation or extraction from Te target solutions. In some cases, addition of carrier may be specifically required to provide the product radionuclide in the appropriate chemical form, as in the addition of F_2 for the production of ^{18}F labeled F_2 for use in the synthesis of ^{18}F labeled 5-fluorouacil or 2-deoxy-2-fluoro-D-glucose. The production of "carrier free" radionuclides has received a great deal of attention, but recent emphasis has focussed upon the difficulties of assuring that a given product is truly free from stable isotopes. If no

carrier has been specifically added during processing and the amount of stable isotope is analytically undetectable, the designation "no carrier added" is preferred. If the level of carrier is known, the specific activity can then be stated [23]. In the following chapters both cation and anion exchange resins will be investigated for carrier-added and carrier-free separations of ^{103}Pd from Ag and Rh targets.

CHAPTER 2

SEPARATION OF Pd-103 FROM Ag AND Rh FROM SILVER TARGETS

2.1 INTRODUCTION

Most methods so far developed for ion exchange separation of Ag employ anion exchange resins on which this element can be rather selectively sorbed as an anionic complex containing chloride, bromide, or thiocyanate ligands. Selective separation of Ag on cation exchange resins can in most cases be achieved in the presence of neutral complexing agents for Ag or the other elements. Chelating resins have not found broad application in the analytical chemistry of Ag(I). The distribution coefficients of all elements on these resins are highly pH-dependent [25]. For the separation of Ag from a synthetic mixture including Pd(II), the Bio-Rex 70 carboxylate resin and Dowex A-1 have been used. The latter, which is similar to Chelex 100 [24,25], is suitable for the preparation of carrier-free ^{111}Ag from neutron irradiated Pd [25]. A dilute nitric acid (0.1-0.5 M) solution is necessary for the separation. In this medium the distribution coefficient of Ag is 5. No attempt has been made to elute the Pd.

Production of ^{103}Pd from ^{nat}Ag targets using the 66 MeV proton-induced reaction at the iThemba LABS was first studied by Fassbender *et al.* [8]. In this study a radiochemical separation employs two different ion exchange resins: Chelex 100 for retention of Pd and Rh and cation exchange resin AG 50-X8 for separation of Pd from Rh using thiourea solution. In another study to produce ^{103}Pd from ^{nat}Ag , a 140 MeV proton-induced reaction was reported by Mausner *et al.* [27]. It is claimed that by using only the Chelex100 (but employing two columns of different size), the Pd was separated from Rh and Ag (as well as Ru and Tc), which is inconsistent with the aforementioned report.

A distribution coefficient analysis of most elements in nitric acid media have been made and the results presented in the periodic table format by Faris *et al.* [28,29]. In all concentrations of nitric acid, 1-14 M, no Rh or Ag is sorbed to any significant degree. Investigations have shown that Ag^+ is the main species in aqueous nitric acid solutions. The dissociation constant of the neutral complex $AgNO_3$ in solutions is 0.51 (or $pK_{diss.}$= -0.29) [30]. In aqueous nitric acid solutions, ranging from 0.5 M to 14 M, however, the distribution coefficients of Ag were found to be in the range of ~0.2 to ~0.4 [25]. In $NaNO_3$ solutions of comparable concentrations, these distribution values are somewhat higher, but do not exceed unity. The distribution coefficient for Pd reaches a maximum of about 100 in 2 - 3 M nitric acid. The difference between the distribution coefficients of the three elements in HNO_3 is large enough to expect a good separation of Pd from the two elements.

2.2 EXPERIMENTAL

To develop a separation technique for a new radionuclide production, several routes are usually considered and many experiments are performed to find the best one in terms of the recovery of radionuclide of interest, chemical and radionuclide impurities in the final solution resulting from target material and substrate, time efficiency, the volume of solution for the separation and ease with which the procedure can be achieved in the hot cell. It is, therefore, advisable that, before any radiochemical separation in a hot cell takes place, these measurement experiments should be performed with natural elements (or "cold runs"). The selection of a measurement procedure and technique must be compatible with the instruments available at that particular laboratory. This procedure would also be used for routine chemical quality control (Chapter 1, Section 1.4). The ICP-OES technique with high linear dynamic range, a powerful tool for multi-element analysis, makes it possible to measure the analyte with low concentration in the presence of high concentration of the matrix species. This technique was thus employed for measurements of natural elements, using two instruments.

In this investigation of the separation by ion exchange chromatography, three different resins with similar procedures were used and only the last procedure using AG MP-1 is presented here.

2.2.1 Reagents and equipment

The AG MP1 anion exchange resin (100-200 mesh, chloride form) was purchased from Bio-Rad Laboratories and high purity (99.999%) silver metal from BDH Chemical Ltd., Pool, England. All chemicals were of analytical grade and water obtained from a Milli-Q system with 18 MΩ/cm resistance.

Two ICP-OES instruments, namely, a Varian P400 and a JOBIN YVON model ULTIMA (purchased recently) were used. This technique was also used for distribution coefficient measurements (all by the Varian P400).

For the determination of Pd, in presence of Rh and Cu, 0.5 M HCl was used as the medium, while 0.5 M HNO_3 was used for the determination of Pd from Ag target solutions. In each experiment, samples from effluent and eluate were measured and compared to the sample taken from the original solution. When it was necessary, a solution was diluted or evaporated, followed by the adjustment of the acidity to 0.5 M. For example, the ammonia solution (for the elution of Pd) was evaporated to a certain volume and then hydrochloric acid or nitric acid was added.

The most sensitive emission lines of the elements were selected for the ICP measurements; 340.458 nm, 343.489 nm, 324.754 nm, and 328.068 nm for Pd, Rh, Cu, and Ag, respectively. In the region of Pd (340.419 nm - 340.497 nm), the other elements do not have any emission lines.

The radioactivities induced in the targets were measured with two accurately calibrated HPGe detectors, coupled to a SILENA 16k multi-channel analyser (MCA) system. The detectors used were the standard intrinsic Ge γ-ray (ORTEC, with a Be window) and a planar X-ray (APTEC). Each detector was mounted at the end of a 2 m long bench with a movable holder. This set-up enables the setting of the source-to–detector configuration with a high degree of repeatability. The MCA system has 16384 channels of which 4196 were available for a single spectrum. The resolution for the γ-ray detector was 1.7 keV FWHM at 122 keV and 0.92 keV FWHM at 21 keV and 1.22 keV FWHM at 40.1 keV for the X-ray detector. The energy calibration was accomplished by the use of sources which have several peaks of accurately known energies spread across the entire region of interest. In this case the region of interest was between 11 and 1408 keV. The use of ^{241}Am, ^{152}Eu, and ^{133}Ba sources, therefore, was appropriate because they have peaks spread across the entire region of interest. These sources were prepared, specially, for this experiment, at the CSIR National Metrology Laboratory, South Africa.

In order to generate good statistics, high counting rates were preferred. The total system dead time was kept below 3% and this was accomplished by choosing an appropriate distance between the sample and the detector.

2.2.2 Column ion-exchange procedure

The resin was first converted to the nitrate form in a large column (20 cm × 3 cm). For the conversion, 3 M nitric acid was used and at the end of the process, the eluate negatively tested for chlorides by addition of a dilute solution of $AgNO_3$. Finally, the acid was eluted with water prior to storage of the resin. This resin was used for the separation experiments.

A column (20 cm × 0.8 cm) was packed with the resin and preconditioned by passing 100 ml 3 M nitric acid through the column. The sample was prepared by dissolving 16 g granular Ag in 30 ml 12 M nitric acid while heating. After complete dissolution, heating was continued to evaporate the excess nitric acid until a white precipitate appeared. The residue was then cooled down. To this solution, while stirring, 50 ml 0.5 M nitric acid solution containing 1 mg Pd, was added to dissolve the precipitate. This solution was loaded on to the column using a peristaltic pump with a flow rate of 1.5-1.8 ml/min. 120 ml 3 M nitric acid was then pumped through the column for the complete elution of Ag and Rh. The acid was removed by elution with 100 ml distilled water; Pd was finally eluted with 150 ml 5% ammonia solution. The ammonia solution was evaporated, to drive off the excess ammonia, and added to the water eluate.

Natural Pd was determined by the ICP-OES technique, while activity measurements were performed using Gamma Spectrometry. Natural silver ions were only qualitatively indicated by precipitation with 0.05 M hydrochloric acid solution.

2.3 RESULTS AND DISCUSSION

To separate Pd selectively in the presence of a large amount of Ag target material, ion exchange chromatography was chosen and three ion exchange resins studied before the best of them, in terms of Pd recovery, was finally selected.

2.3.1 Chelating resin, Chelex 100

To develop the previously mentioned method tested at iThemba LABS [8], several experiments were conducted with the Chelex 100 resin using a small column (3 cm ×1 cm). The sorption and elution of Pd in 0.5 M nitric acid solutions were studied. As expected, Pd was strongly retained by the resin and 10 M HCl solution was used to elute it. The recovery of Pd was low due to the too high affinity of the resin for the metal ions. Even by using a very small column (2 cm × 0.3 cm) and up to 1 mg Pd carrier, the recovery was not more than 60% with 100 ml 10 M HCl as eluent.

Chelex 100 is an iminodiacetate chelating resin (Fig. 2.3.1.) that reacts with heavy metal ions by simple ion exchange at low pH values, while tridentate (O,N,O) chelation dominates at higher pH. At intermediate acidities both mechanisms are appliable [25], hence, at low pH, where the amine N of the resin functional group is protonated and the carbonyl groups neutral, it acts similar to a weakly basic anion exchange resin but now containing a tertiary amine group. Considering the fact that in 0.5 M nitric acid most of the Pd ions, if not all, are present as anionic nitrato complexes, it can be understood that most of the Pd is associated with protonated nitrogen and it is very difficult to attain complete elution of Pd (sorbed as $Pd(NO_3)_4^{2-}$). Furthermore, it has been shown that elution of heavy metal ions by HCl solution (> 2 M), that forms anionic chloro complexes (e.g. $[PdCl_6]^{4-}$ and $[PdCl_4]^{2-}$), is incomplete. Again, the ion pair association involves the anionic metal complex and the ammonium group on the resin [25]. When we employed weakly basic anion

exchange resin AG3-X4 (that also contains a tertiary amine functional group at low pH) the elution of Pd was also poor.

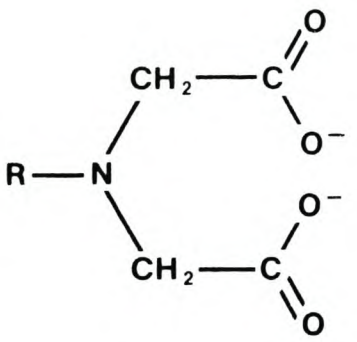

Fig. 2.3.1. Functional group of Chelex 100

2.3.2 Strongly basic anion exchange resin AG1-X8

In the light of the negative results mentioned above, a strongly basic anion exchange resin was employed for the separation and AG1-X8 was first resin chosen for this purpose.

In the first experiments only Pd-containing solutions in 3 M nitric acid (25 ml) were used. The solutions containing 1 mg Pd, transferred through the column (5 cm × 1 cm I.D.) at a flow rate of approximately 2 ml/min. Pd was quantitatively sorbed on the resin. For the elution of Pd very dilute nitric acid solutions, from 0.01 to 0.1 M were used because it was believed that in such dilute solutions the neutral complex $Pd(NO_3)_2$ would form [26] that could easily be eluted from the resin. This was observed when washing the resin with water - the colour of solution under the column changed to yellow, an indication of Pd elution by the water. Indeed, in some experiments, when using up to 50 ml water, it was observed that about 70% of original Pd was collected in the water eluate and 90% in total by using 0.02 M nitric

acid after the water. The results seemed acceptable until a mixed solution of Ag and Pd was used for the separation. Then part of the Pd was not sorbed and passed into the effluent - the more Ag in the solution, the less the sorption of Pd. The column was then replaced by a 10 cm × 1 cm column and, again, when the amount of Ag was increased up to 16 g (the mass of a real target) and, consequently, the volume of the solution increased to approximately 75 ml, almost 50% of Pd passed directly through the column. The high Ag concentration probably reduced the distribution coefficient significantly and the Pd moved further down the column than expected. The problem was solved by using a much longer column, 20 cm × 0.8 cm. A peristaltic pump was employed for transferring the solutions to the column. Although with the new column a complete retention of Pd was obtained, the elution, when using 100 ml water followed by 150 ml 0.02 M nitric acid, was not as effective as before (the first column), furthermore, the results were not reproducible. This could be attributed to the length of the column. For this reason the dilute nitric acid solution was replaced by 150 ml of 5% ammonia solution as the eluent. After obtaining good results with the ammonia solution, the experiment was repeated. The results of 10 experiments using 16 g Ag, as the target, showed a recovery of 96.5 ± 4.2% of Pd. Presence of Ag in the final solution was simply tested by adding dilute HCl (to form AgCl precipitate). Rh - with a concentration in the original solution of 2 ppm - was found to be less than the detection limit of the ICP spectrometer. The radionuclidic impurities of these two elements in the final solution, however, was later measured by gamma spectrometry.

The resin was regenerated with 6 M nitric acid solution. It was observed that the recovery of Pd decreased to about 70% when the resin had been regenerated without emptying the column, hence, after each experiment the column was emptied of the resin, the latter first washed with 6 M nitric acid, followed by water, re-packed in the column, regenerated with 100 ml of 6 M nitric acid and finally washed with distilled water. In this way the packing had the same structure as before and, indeed, afterwards the results of Pd recovery was reproducible. It should be mentioned that in practice, especially, when working with high level radioactivity, the same resin is not re-used. Although the resin is very resistant towards radiation, it is poisoned by huge amount of silver and poor recovery can be expected.

The reason for adding 50 ml of 0.5 M nitric acid (containing 1 mg Pd) to the saturated solution of dissolved target is, firstly, to dissolve the silver nitrate precipitate completely and, secondly, also to adjust the concentration of NO_3^- ions to about 3 M. This was the concentration of nitric acid that had already been used for sorption of Pd. It is shown that the concentration of nitrate ions determines the distribution coefficient values of Pd on strongly basic anion exchanger resins (Section 2.1) and not the acid concentration itself [27].

In early experiments it was observed that washing the column with small amount of distilled water (ca 50 ml) was not enough to wash the nitric acid completely off the column. As a result, when eluting Pd with ammonia solution, the vapour of ammonium nitrate (formed in the column) disturbed the packing of the resin and, thereby, the recovery of Pd.

To find the optimum volume for the elution of palladium an elution curve was determined, using 100 ml distilled water followed by 150 ml 5% ammonia solution. 10 ml aliquots were selected for the curve and, for better observation of the differences between the concentration of aliquots, emission intensities in ICP measurements were used instead of concentration. Fig. 2.2.2 shows the elution curve. There are two peaks which indicate either elution of two different kinds of complexes of Pd formed on the column or the existence of two different complexes in the original solution. The small peak at the beginning of the curve (in the first 30 ml of water) is probably $Pd(NO_3)_2$ and the second one $[Pd(NO_3)_2(NH_3)_2]$ or most probably $[Pd(NH_3)_4](NO_3)_2$ [31]. It can be seen that for the complete elution of Pd, less than 100 ml ammonia solution suffices.

After these successful results, using natural Ag, Rh and Pd, a radiochemical processing panel system was designed for activated targets and installed in the hot cell. Fig. 2.2.3 shows the flow diagram of the system. All numbers in circles indicate 3-way valves that are opened by a manipulator. The target is dropped into the "reaction vessel" by the manipulator and heating and stirring is started. The concentrated nitric acid (12 M) and Pd in 0.5 M HNO_3 for dissolution of target and dissolution of the formed precipitate, respectively, is transferred from the "Outside

Line" through valve 1, via the peristaltic "Pump", to the "Reaction Vessel". All nitric acid solutions, ammonia and water for preconditioning the resin, elution of Ag and Rh, and elution of Pd, are pumped from outside through the valves 2, 6, and the line "Load 1", valves 2, 7, and 8 to the column. The solution of dissolved target is pumped from the reaction vessel to the column through valves 3, 2, 6, line "Load 1", valves 7 and 8. If somehow the filter is blocked, the solution is transferred through valve 4. Valve 9 is used for the sampling of the original solution to compare to the final solution for recovery purposes and valve 10 is used for collecting both the waste and the product (as final solution). The line "Load 2" is used as a spare line for "Load 1".

Three separation experiments were performed in the hot cell on bombarded Ag targets three days after bombardment. For calculating the yield of the radiochemistry and radionuclide impurities by γ-spectrometry, one sample was taken before and one after the separation and compared to each other for Pd, Ag and Rh. The energies of 84 keV (100% abundance), 344.5 keV (41.6% abundance), and 306.9 keV (86.3% abundance) were used for ^{100}Pd, ^{105g}Ag, and ^{101m}Rh measurements, respectively. Using 100 ml water and 150 ml 5% ammonia for elution (as used for natural targets), the average recovery was about 80%. Counts for ^{105g}Ag and ^{101m}Rh were found to be at a background level. The effluents were also measured to ensure that the Pd did not pass into it. A recovery of 90% was obtained only after using 300 ml of the ammonia solution. These results, in which the recoveries were less than those obtained from cold tests, indicated that there is a tailing phenomenon inhibiting complete elution. When deriving the aforementioned elution curve, it was assumed that the intensities of the last 10 aliquots (the tailing) were instrumental drifts, mainly because of the high recovery that had been obtained before. The difference between ICP measurements and those obtained from gamma spectrometry can be explained by the fact that elution of Pd was never complete with the AG1-X8. This result also reveals

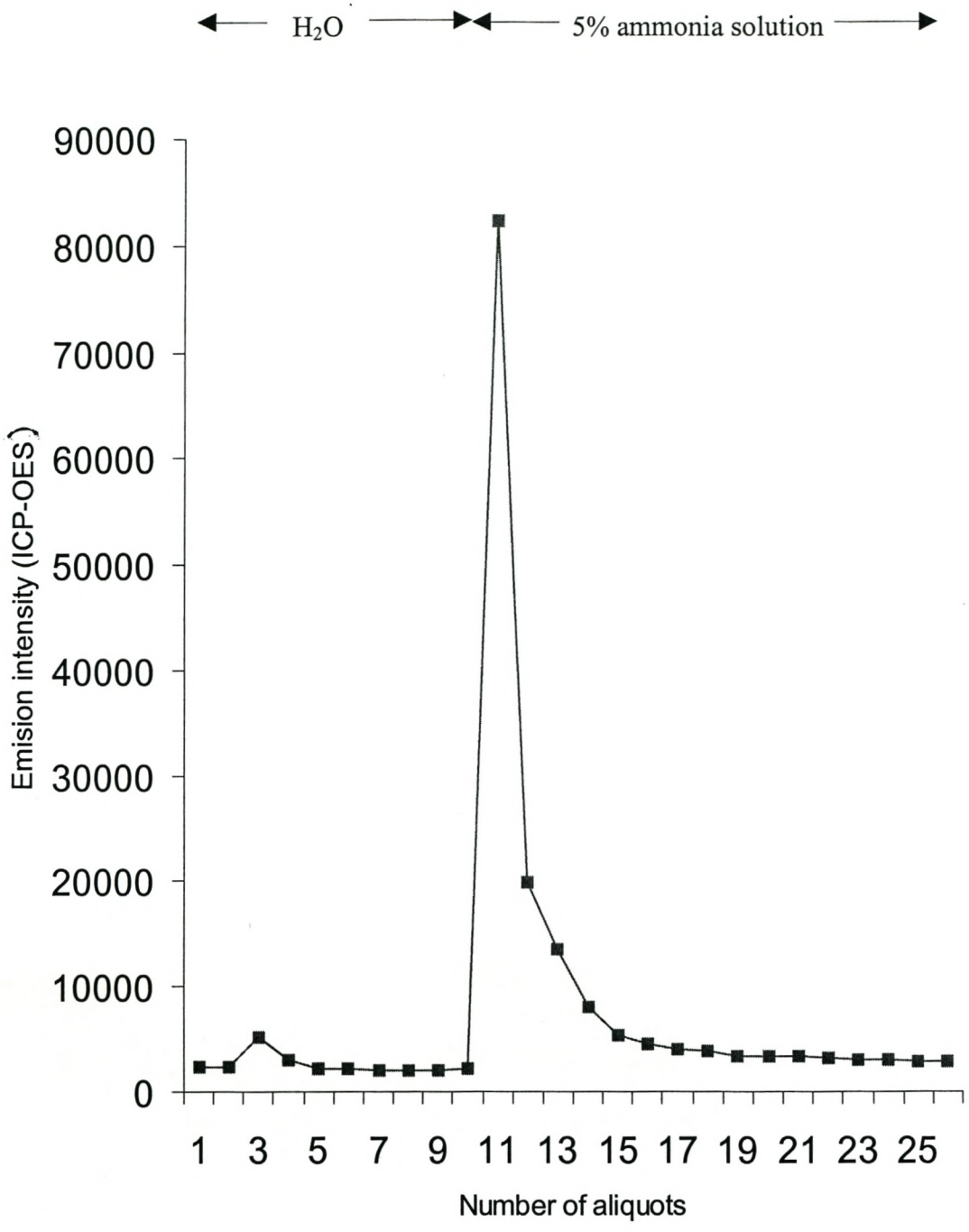

Fig. 2.2.2. Elution curve of Pd on AG1-X8 resin (100-200 mesh; 20 cm × 0.8 cm column; flow rate 1.6 ml/min; 100 ml water followed by 150 ml 5% ammonia for elution).

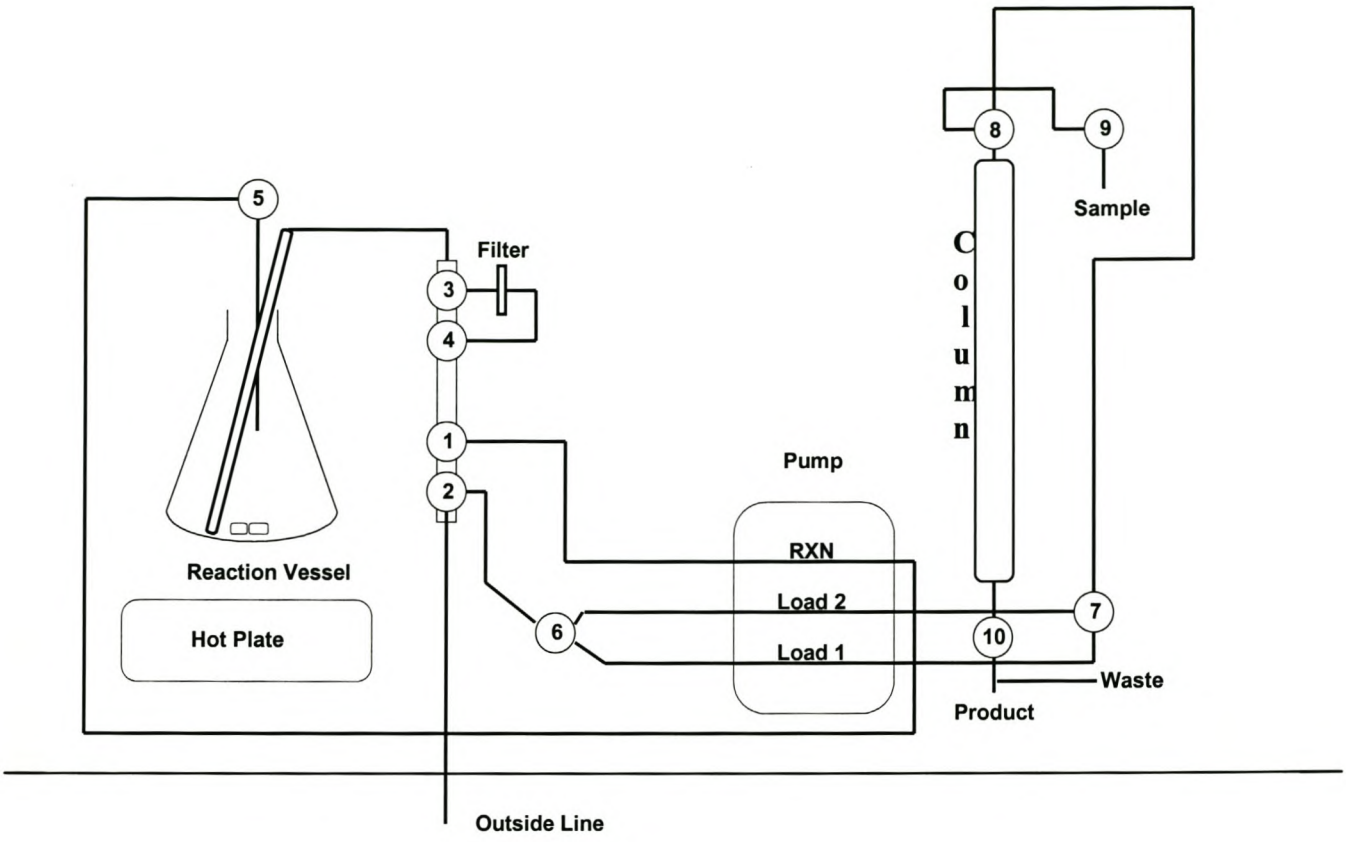

Fig. 2.2.3. Flow diagram of radiochemical system for production of ^{103}Pd from the Ag targets.

that regeneration of the resin was not complete, either. Consequently, after each experiment some Pd retained on the resin, which was eluted in the following experiment. This cycle, retention and following elution of a constant amount of Pd, resulted in the high recovery with low error margin. This explanation was later on confirmed when separating of Pd from Rh targets in 3 M HNO_3 (Chapter 4, Section 4.3.4); a new column was used in each experiment.

2.3.3 Macroreticular anion exchange resin AG MP-1

To overcome the above mentioned incomplete elution, the macroreticular anion exchange resin AG MP-1 was then investigated as a substitute for the AG1-X8 resin. This kind of resin offer a number of advantages over the conventional gel-type resins. Having large discrete pores means that ions with a high molecular mass can be more completely removed from solution and more completely eluted from the resin during regeneration than would be the case with other materials. Although the macroreticular resins, on the whole, have a somewhat lower capacity than the gel-type resins, this is often offset by the fact that they will effect removals not possible by the gel-type resins. Although the distribution coefficients of the anionic species are substantially higher, they are more readily eluted since the kinetics resembles the 4% cross-liked anionic resin AG1-X4. With these advantages it would be possible to use even smaller columns and/or higher flow rates. The procedures for the preparation of the resin and the column preconditioning were the same as described for AG1-X8 (previous section). After obtaining a recovery of 97.4% from a solution of natural Pd and Ag, using the new ICP instrument, an elution curve experiment was conducted. This time ^{103}Pd, obtained from a previous production, was employed as tracer. As eluents, 150 ml water followed by 350 ml 5% ammonia solution were used. Each aliquot contained 10 ml solution. The X-ray detector was used for counting the samples and counting time was 100 seconds. The elution curve is shown in Fig. 2.2.4. The shape of the curve is very much like the one obtained for AG1-X8 except that the Resolution is higher. It can also be seen that most of the Pd is collected only in one fraction (the third aliquot of ammonia) and that there is no longer any tailing.

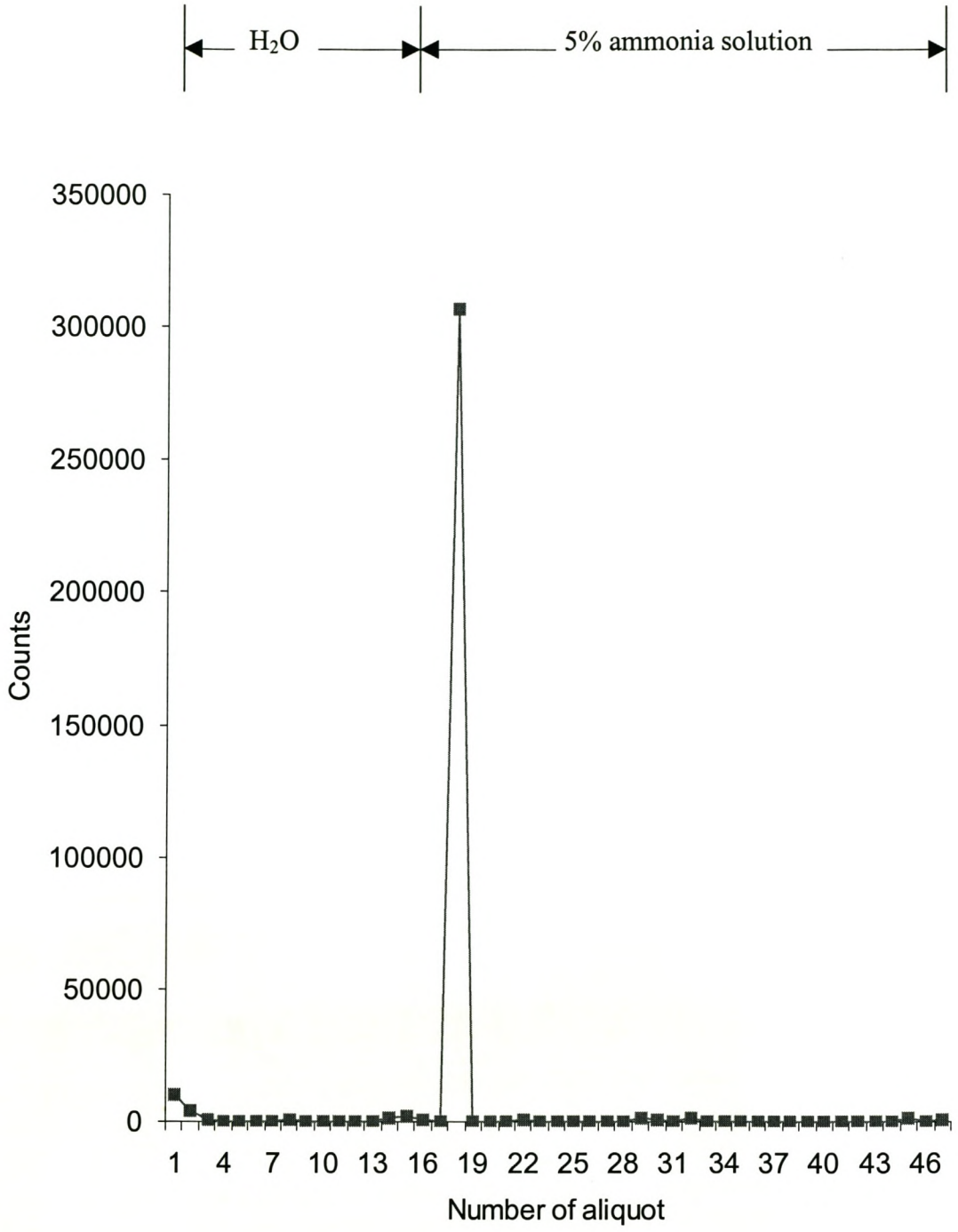

Fig. 2.2.4. Elution curve of Pd on AG MP-1 resin (100-200 mesh; 20 cm × 0.8 cm column; flow rate 2 ml/min; eluent 150 ml water followed by 350 ml 5% ammonia solution).

The main problem associated with the production of ^{103}Pd from natural Ag using a 66 MeV proton beam is a high radionuclide impurity of ^{100}Pd (half-life 3.63 d), which decays to ^{100}Rh (half-life 20.8 h). The practical yields at the end of bombardment (EOB) for this production route are 25.1 and 3.3 MBq/μAh for ^{103}Pd and ^{100}Pd, respectively. The maximum yield of ^{103}Pd production from a Rh target (EOB), which was calculated by Hermanne *et al.* (see also Figures 1.3.1 and 1.3.2, Chapter 1.) [10-12], is about 11 MBq/μAh. It can be shown (Table 2.3.1) that 20 days after bombardment (for a silver target), the radionuclide impurities of ^{100}Pd is decreased to a reasonable level of about 0.5%. After this period, the yield from the Ag target is very close to that of ^{103}Pd from a Rh target. For a routine production of ^{103}Pd from a Ag target by high energy cyclotron, although at the expense of more than a half of the original activity, it is advisable to carry out the radiochemical separation at least 20 days after bombardment.

Table 2.3.1 Production yield of Pd-103 and percentage of Pd-100 present (as the radionuclide impurity) from a Ag target.

Time	Pd-103 Yield (17 d) (MBq/μAh)	Pd-100 Yield (3.63 d) (MBq/μAh)	Impurity of Pd-100 (%)
EOB	25.1	3.3	11.6
3.6 d	21.65	1.65	7.62
7.2 d	18.67	0.825	4.42
10.8 d	16.10	0.41	2.56
14.4 d	13.90	0.21	1.47
17.0 d	12.55	0.105	0.84
20.0 d	11.11	0.053	0.47

2.4 CONCLUSIONS

The results of test runs obtained from the newly designed radiochemical unit show that for a high-energy cyclotron, a Ag target can be used to produce ^{103}Pd via the proton-induced reaction ^{nat}Ag (p,xn) ^{103}Pd. Although the radionuclidic impurity (^{100}Pd) is ca 11.6% at EOB, it can be reduced significantly to about 0.8% by processing the target (to recover ^{103}Pd) after about one half-life of ^{103}Pd ($t_{1/2}$ = 17 d). This will, however, result in a lower yield of ^{103}Pd but the yield is then about the same as for a Rh target. The big advantage is that a Ag target costs much less than a Rh target and the dissolution of Ag is easy to accomplish in a hot cell compared to the tedious dissolution method of a Rh target. Furthermore, Rh has to be recovered for re-use as a target because of its price.

CHAPTER 3

ELECTROPLATING OF Rh ON A COPPER SUBSTRATE FOR PREPARATION OF Rh TARGETS AND DISSOLUTION OF Rh BY USING ALTERNATING CURRENT

3.1 INTRODUCTION

For some compact cyclotrons, the target materials are usually deposited on a copper substrate, preferably by electroplating [9]. The plating must be of such quality that during transportation and heating in the bombardment process it is retained on the substrate. To separate the Pd produced by the bombardment, the electroplated Rh has to be dissolved and it is an advantage if this solution can be used directly for the separation.

Rhodium is a precious metal, very stable to oxidation, hard and highly reflecting, and its density is only about half that of platinum. It is, therefore, not surprising that there could be a significant market for rhodium coatings and that almost all commercial electroplating procedures are patented. Some years ago rhodium was the precious metal most frequently electroplated, usually employing plating baths with sulphuric or phosphoric acid electrolytes. This situation has, however, changed mainly because engineering applications of precious metals have become much more important. This generally requires relatively thick coatings (above 3 μm) and a high rate of deposition; rhodium coatings from acidic baths become highly stressed when they are deposited to such thickness, while the rate of plating is low [32]. Rhodium electroplating baths and, for the first time, the fundamental chemistry and electrochemistry of Rh(III) in acidic sulphate and chloride media have been

investigated by Pletcher *et al.* [32,33] and the deposition analyzed by means of scanning electron microscopy.

Depending on the application, electroplating of Rh in industry is achieved in various ways. This includes a wide range of Rh concentrations from 0.1 to 30 g/l, different additives for reducing tension, current densities between 1 mA/cm^2 and 1.5 A/cm^2, temperatures from 20 to 90 ^0C and the use of different acids such as sulphuric, phosphoric and perchloric acids [34-38]. Due to problems associated with electroplating on pure Cu, nickel-electroplated brass or brass have generally been used as substrate. To avoid more radionuclidic impurities, it is desirable to employ very pure Cu as the substrate for Rh target.

To avoid the problems with chloride baths mentioned above, most electroplating baths for rhodium metal, particularly for the production of the thick deposits employed in engineering and other industrial applications, are utilizing acidic sulphate media.

For the electroplating of 0.1 mm thick Rh on a copper substrate as a target, Chung *et al* [9] used an electrolyte in which the main component is rhodium(III) chloride hydrate, $RhCl_3.3H_2O$, (no details about possible other additives were mentioned). This electroplating is performed at 45^0C with a current density of 0.2 A/cm^2 using a periodic reverse plating instrument (IBA, the manufacturer of 30 MeV cyclotrons, provides this electroplating power supply to its customers).

Pure compact rhodium is resistant to oxidation by acids. It can, however, be dissolved in acid after melting it with tin. Palladium in this solution is present partly in a colloidal state causing problems during the separation. Furthermore, fusion with alkaline hydroxides, with pyrosulphates, or chlorination can be employed to dissolve rhodium, but all these methods are difficult to perform in a hot cell. The most suitable method is the electrolytic dissolution by applying alternating current in hydrochloric acid solution. When other acids or diluted hydrochloric acid (below 6 M) are used, the rate of dissolution decreases considerably [13]. It takes about 16 hours to dissolve an 8 g rhodium target with a surface area of 32 cm^2. In another study, for the production of ^{101}Pd from Rh targets [39], the alternating current electrolytic dissolution method in

6 M HCl is employed for dissolving a metallic Rh foil (0.0125 cm thick and 0.63 cm diameter). With a current density of 0.4-0.6 A/cm^2 the process needs about 4 hours to complete.

3.2 EXPERIMENTAL

3.2.1 Electroplating of rhodium on copper

3.2.1.1 Reagents and Equipment

The solutions were prepared with water obtained from a Milli-Q purification system and chemicals of analytical grade.

3.2.1.2 Preparation of the bath solution

100 mg $RhCl_3.3H_2O$ was dissolved in 5 ml 1 M NaOH solution and heated until a yellow hydrated precipitate of rhodium(III) oxide, $Rh_2O_3.xH_2O$, was formed. This precipitate was filtered off and then washed with hot water repeatedly until the wash solution tested free of Cl^- ions (using 0.01 M $AgNO_3$ solution). The rhodium oxide was then dissolved in warm 1 M $HClO_4$ solution and the resulting solution cooled and diluted with distilled water and adjusted to 0.5 M $HClO_4$ (200 ml). For the electroplating step, 20 ml of this solution was used in the bath.

3.2.1.3 Electroplating

The surface of the copper was polished by rubbing forcefully using 400, 800 and 1200 grade emery papers. The electroplating was then carried out in a 3 cm-diameter cylindrical cell made in a cube with two circular holes (diameters 1 and 2 cm) on two opposite sides. A graphite sheet was placed over the larger circle and acted as the anode, while the copper substrate was placed over the small circle, acting as the cathode. The electrodeposition was performed at room temperature, at a constant current of 0.5 A for 1 hour, without stirring the solution.

3.2.2 Dissolution of the electroplated rhodium by alternating current

3.2.2.1 Reagents and equipment

A 50 Hz variable alternative power supply POWERSTAT (The Superior Electronic Co., Bristor, Conn. U.S.A) coupled with an electronic timer (RHOMBERG Electronics, RSA) was used for the dissolution.

3.2.2.2 Dissolution procedure

The Rh-electroplated copper substrate and the graphite sheet, which were in oval shape, were clamped at the two sides of the electrolysis cell (described in the previous section). The cell was then filled with 20 ml 6 M HCl and the current was adjusted to *ca.* 1.6 A. During the 30 minutes used for electrolysis, the temperature was raised up to 70^0C.

3.3 RESULTS AND DISCUSSION

3.3.1 Electroplating of rhodium on copper

This section was seen as very important, as rhodium is a precious metal and, generally, in an electroplating process Rh is not completely depleted from the bath and the electrolyte must be re-used. Using additives might advance the quality of the plating but they are susceptible to oxidation, reduction and decomposition and can negatively effect the quality of the plating, should the electroplating process take place a few times. To avoid further complications it was deemed necessary to find an electrolyte free from any additives so that it can be used as many times as possible.

The surface area of a typical target (see also reference [9]) is 12 cm^2 and it can be shown that for electrodeposition of 1 g Rh with the low currents used by Pletcher *et al.* (0.5 - 1 mA/cm^2) [32,33], even with 100% current efficiency, more than 60 hours would be required to deposit this mass quantitatively. For our purpose this was totally impractical. Although commercial electroplating baths for rhodium generally employ a strong acid electrolyte [32-35] leading inevitably to a low current efficiency due to competing H_2 evolution, on the whole the deposition rates are better than that of using low acid concentrations with very low current density of 1 mA/cm^2.

Nevertheless, several experiments were performed with chloride baths at pH 2 - 4 with rather high currents (from 50 to 10 mA). In these experiments the $RhCl_3.3H_2O$, which is commercially available and easily dissolves in water, was used. To convert this compound to the hexachlororhodate complex (as used by Pletcher *et al.* [32]), it was dissolved in 6 M HCl and aged for 2 days [25]. The solution was evaporated to a very small volume, dissolved in water and its pH adjusted with 1 M NaOH to fall between 2 and 4. After 15 minutes, only with the low current (10 mA) a black plating was obtained, on which some black precipitate occurred. Some colloidal precipitate appeared in the solution. With higher currents no real plating formed and a black precipitate on the electroplating area was easily removed by hand. It is common

knowledge in the precious metal plating industry that chloride baths do not lead to highly reflecting and good quality rhodium deposits. The reasons are clear: smooth and uniform electroplates are unlikely to be formed in conditions where the substrate surface is disrupted by corrosion or cementation reactions. The chloride ion accelerates the corrosion of most metals, especially copper, where the chloride ion is a strong ligand for Cu(I) [30]. Of course, shifting the potential of the substrate corrosion towards more negative values or increasing the kinetics of corrosion also accelerates the rate of the cementation reaction ($Rh(III) + 3Cu + 6Cl^- \rightarrow Rh + 3CuCl_2^-$). In contrast, the deposits on the inert substrate are excellent. This suggests that chloride baths are suitable for rhodium plating if used in conjunction with an appropriate undercoat of an inert material. Gold seems to be a suitable candidate [32].

Several experiments were conducted with sulphate baths and the results compared to those obtained with chloride baths. For the preparation of rhodium sulphate, from the rhodium chloride, the same procedure was used as described for perchloric acid baths (Section 3.2), except that the intermediate rhodium oxide hydrate was dissolved in 1 M sulphuric acid solution. This solution was divided into two parts. The first solution was directly used for the electroplating; with a current of 100 mA. The appearance was uniform, bright and a little reflecting. The pH of a second solution was increased to 3 by addition of 1 M NaOH and then used for electroplating at a constant current of 50 mA. Despite this rather high current (compared to 1 mA mentioned above), the plating was adherent, gray and not reflecting.

Suitable Rh coatings on Cu, Ni, Ag, and Au have been obtained from $Rh(ClO_4)_3$ in $HClO_4$ baths [34]. The electroplating is performed at room temperature using a current density of 1 A/cm^2 and a graphite sheet as the anode; a deposition rate of about 5 μm/hr was reported. It can be shown that the current efficiency is about 0.4% and that for preparation of a 1 g target, the electroplating procedure would require about 20 hours. The same method was followed in the present work. The rhodium oxide hydrate was dissolved in 1 M perchloric acid solution to prepare the needed electrolyte. The quality of the plating was similar to that obtained in the 1 M sulphuric acid bath. When this bath was used with a lower current, 0.5 A, a uniform, adherent and shiny plating was obtained. The quality of the platings was tested

mechanically and also judged by appearance. If the appearance of the plating was rather reflecting and it was not removed by scrubbing using a soft abrasive, this plating was considered suitable for targetry purposes. This last procedure was, therefore, chosen as the electrodeposition method for target preparation.

After each experiment a small amount of graphite was removed from the anode surface colouring the bath dark. This solution was filtered and the filtrate analysed for rhodium content. The results of these measurements showed less than 15 ppm Rh in the baths, which meant that almost all the rhodium was consumed. The filtrate can be used for the next electrodeposition, however.

In the first experiments simply a beaker was used as an electrolysis cell, a rectangular bar of copper as the cathode and a rectangular bar of graphite as the anode. The distance between the two electrodes was approximately 3 cm. The platings obtained were strong and reflecting. Since the electroplated rhodium was supposed to be dissolved by an alternating current (see next section), the same cell arrangement was used again for the dissolution. During the electrodissolution process in 6 M HCl, it was observed that after a few minutes undissolved rhodium were removed as shiny flakes from the surface of the copper substrate with only the copper dissolving. This phenomenon can be explained in terms of non-uniform plating on the copper substrate, primarily resulting from the shape of the cathode. The HCl solution penetrated into the copper through the very thin layer of plating and only copper dissolved while the rhodium metal on its surface remained unchanged. It was concluded, therefore, that uniformity of the plating plays the most important role in the dissolution of electroplated rhodium and this prerequisite could not be fulfilled by the too simple cell composition. As a result, an electrolysis cell was designed and made from polyethylene (Fig. 3.3.1). This new cell fulfilled all the electrodeposition and alternating current dissolution experimental requirements.

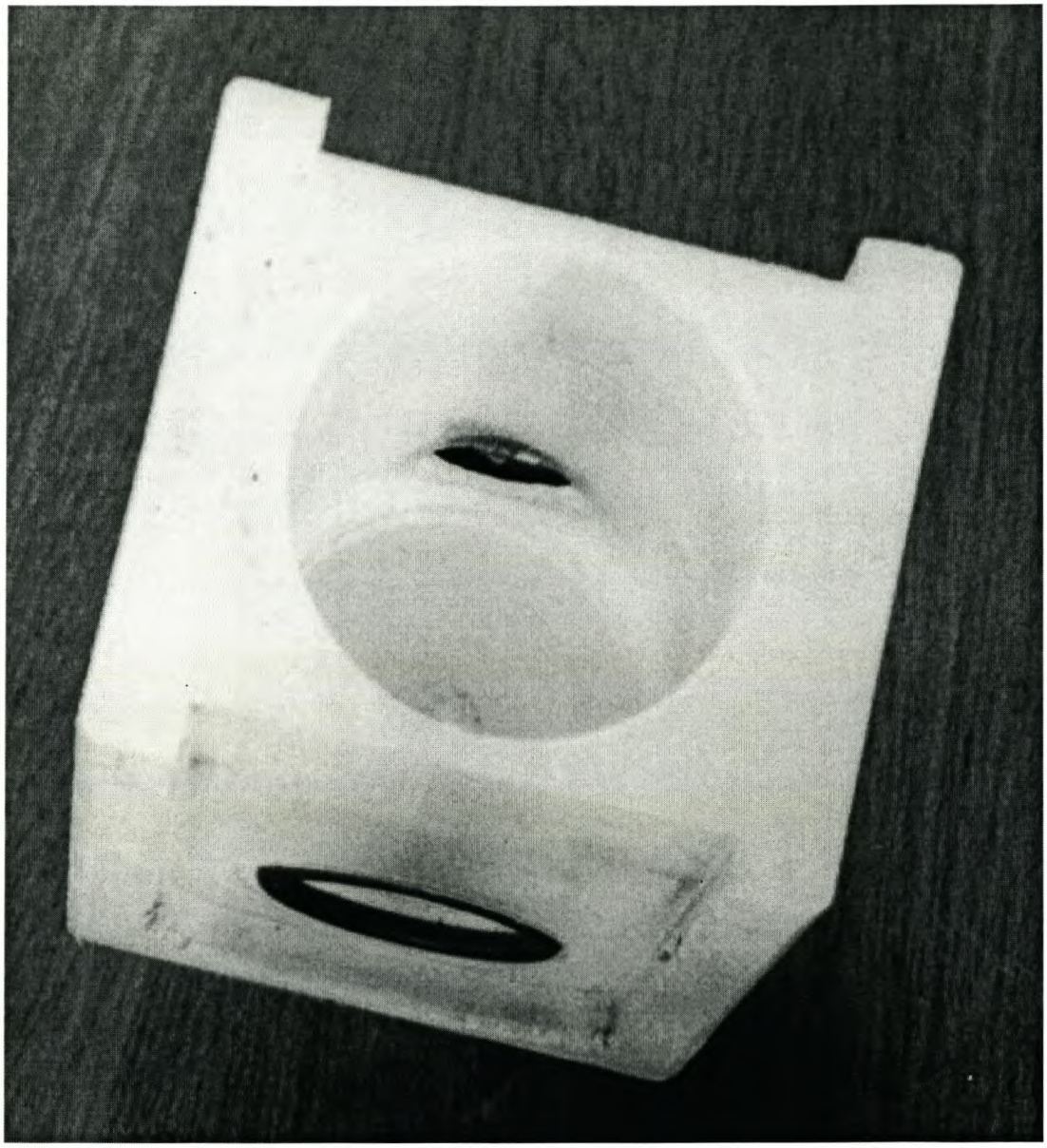

Fig.3.3.1. Electrolysis cell for electroplating of Rh on Cu, Pd on graphite and for electrodissolution of the electroplated Rh on Cu substrate by alternating current.

3.3.2 Dissolution of the electroplated rhodium by alternating current

The surface area of the Cu substrate on which Rh was electroplated was about 0.8 cm^2 (circular with 1 cm diameter, Section 3.2). For the 1.6 A current used, a current density of about 2 A/cm^2 was obtained. Reports on electrolytic dissolution of Rh (references [13] and [39], as examples) suggested that optimum conditions would be obtained using 6 M HCl solution. The rate of dissolution depends on the current density and it is possible to accelerate the dissolution by increasing the current intensity. The mass of Rh plated on the Cu substrate was about 5 mg.

Several experiments were conducted with a low current varying between 0.2 and 1.2 A but no dissolution occurred, despite the fact that this range is more than the required current [13,34]. This could be due to the configuration of the electrolysis cell used in this work; in previous reports the size of the electrolysis cells were not given. On increasing the current to 1.6 A, after a few minutes, the solution became red, indicating the dissolution of Rh. The electrolysis was continued for 60 min. under these conditions. After the first 30 min. the current gradually increased. It can be explained that when Rh on the Cu dissolves, part of the Cu also dissolves. The new high current is due to this dissolution of the copper. The surface of Cu became deeply etched and some undissolved flakes of Rh were dispersed in the solution. With the time of electrolysis decreased to 30 min., a very thin and transparent layer of Rh as spots still appeared on the electroplated area, but no Rh flakes were found in the solution. It can be shown that for a real target [9], which contains at least 1 g Rh of 100 μm thickness, the total Rh loss would not exceed 5%. This is a result of the fact that maximum thickness of the plating was about 5 μm (previous section). It is, therefore, possible in practice to avoid the dissolution of copper if care (for example, observing a rapid increase in current) is taken in the dissolution process. This, in turn, can facilitate the radiochemical separation; for example, smaller column and volume of solution for Cu elution.

In addition to the current density, the rate of dissolution depends on the surface area of the electrodes and the geometry of the electrolysis cell. With our electrolysis cell and area exposed to electrolysis, the dissolution rate is about 10 mg/h and, therefore,

for a real target with area of 12 cm^2 the rate would be about 120 mg/h. It implies that dissolution of a target would take about 10 hours.

The most important part of the electrodissolution procedure occurs when the target is mounted on the cell for dissolution. The electroplated area should be perfectly isolated from the copper substrate, because any leakage of hydrochloric acid onto the copper area results in dissolving only Cu with Rh appearing in the form of small flakes. To overcome this problem, the electrolytic dissolution cell should be different from the electrodeposition cell in such a way that the O-ring between substrate and the cell (which protects the Cu substrate from HCl attack) must be thicker than that one used for the electroplating. In this way, despite more loss of Rh, a smaller surface of the electrodeposited area is subjected to the HCl solution which would not penetrate to the Cu substrate. Alternatively, a Rh foil could be used as the target. this means that the targetry system must be changed completely and the recovered Rh from radiochemical separation cannot be re-used making the whole process more costly.

3.4 CONCLUSIONS

The results obtained from test runs in which the electroplating and electrodissolution of Rh were achieved on a small surface area of thickness much less than that for a Rh target (needing at least 100 μm, [9]), are applicable to the preparation of a Rh target and its dissolution afterwards.

Since the electrolyte used for the electroplating is free from organic additives and the Rh not completely used up, the electrolyte bath can be re-used directly. To prepare a new bath with the original concentration of Rh, the recovered Rh from the radiochemical separation must first be converted into $Rh(ClO_4)_3$, as performed in this study, and then added to the already used bath.

CHAPTER 4

CARRIER-FREE ^{103}Pd SEPARATION FROM RHODIUM TARGETS ON AN AG1-X8 ANION EXCHANGE RESIN

4.1 INTRODUCTION

As mentioned briefly in Chapter 2, the second extensively used route for the production of ^{103}Pd is based on proton bombardment of ^{nat}Rh, and a 30 MeV compact cyclotron is very well suited for this purpose. The Rh target can be made from pure metal (as a sheet or lump) [13,39] or Rh can be electroplated on a copper substrate. At present several countries have 30 MeV cyclotrons (manufactured by the IBA company, Belgium), which employs an especially designed copper substrate for the Rh target [9]. The radiochemistry involved in the process comprises separation of Pd from Rh, as the target material, as well as Cu, which also dissolves in the chosen acid medium.

Two general methods - solvent extraction and ion exchange chromatography - are briefly introduced here for the separation of Pd from Rh and Cu revealing also why the present method was chosen for the separation.

Most of reported papers on the production of ^{103}Pd from Rh targets make use of solvent extraction techniques for the separation and purification of ^{103}Pd. A method based on the extraction of palladium with α-furyldioxime into chloroform from acidic solution, was developed by Taraapcik *et al.* [13]. This method is suitable for the separation of palladium from large quantities of rhodium (8 g) in high yield (more than 93%) and also for the preparation of carrier-free ^{103}Pd. It employs several extractions, back extraction, evaporation and mineralisation and is tedious. In the same work, dimethylglyoxime (DMG) complexation has also been utilised for the

extraction of the Pd into chloroform; the low yield observed could probably be due to a large quantity of rhodium forming water soluble complexes with dimethylglyoxime.

According to another publication it is claimed that the DMG used for carrier-free ^{103}Pd production from Rh target [39]. DMG –chloroform has been also successfully used for the separation of Pd from Rh, Ru, and Tc in a HCl-H_2SO_4 system [40] and for separation of traces of Pd from trace amounts of noble and base metals [41].

Solvent extraction studies of Pd with tributhylphosphate (TBP) from hydrobromic acid solution leads to the separation of Pd from Pt metals and some base metals [42]. An average recovery of more than 99% is reported. Pd, together with traces of Cu and Rh, are extracted into 10 ml TBP from a 3 M HBr solution. Palladium is stripped from the organic phase with 2% ammonia solution. The amounts of Pd, Rh, and Cu present in the process are 210 μg, 5 mg, and 2 mg, respectively.

Kumar *et al.* employed o-phenantroline as extrant for microseparation of Pd from Rh and some other metal ions into chloroform [43]. In order to recover the metal ion from the solvent, the combined organic layers are extracted thrice with equal volumes of 25% NH_3 containing 1-2 ml 30% H_2O_2. This method is very selective for the separation of Pd (40-1000 μg) in the presence of Rh and Cu and other ions not exceeding 1 mg.

Rapid and effective separation and determination of Pd in the presence of large amounts of Rh or Cu by extraction with dibenzyldithiooxamide (D_bDO) in chloroform has been reported [44].

Separation of the Pt group elements, including Pd, Rh and Ru by means of ion exchange resins are carried out routinely for the determination of these metals in geological samples, industrial products and synthetic mixtures containing also other elements. Anion exchange resin in hydrochloric acid systems can be effectively used to separate the Pt metals, not only from practically all other elements, but also from one another. Such separations on anion exchange resins are more versatile than those effected by the use of cation exchangers of the sulphonic acid type. The latter,

however, can be employed for the very effective isolation of the Pt metals, as a group, in very dilute HCl media [25].

From published distribution data [25,47,48], it is evident that the Pt metals show only very weak or negligible sorption on strongly acidic cation exchange resins from 0.1 to 3 M HCl solution. In these solutions they are predominantly present as anionic chloro complexes. From dilute HCl solutions Cu(II) is strongly sorbed on cation exchange resins of the sulphonic acid type, e.g. Dowex 50, with a distribution coefficient decreasing from ~10^3 in the 0.1 M acid to values of ~4 and ~2 in 2 and 4 M HCl media, respectively. At higher acid concentrations, i.e. above 6M, the distribution coefficient becomes less than unity. Subsequently, the Cu can be eluted by pure HCl, 2 M for example [25].

Cation exchange behaviour of Pd(II) (our focus here) and other Pt metals, as well as base metals including Cu, was investigated by Paria *et al.* [45]. They used Dowex 50W-X8 and investigated several eluting agents. Pd and base metals are sorbed on the resin while Rh and other Pt metals pass through. Using 4 M ammonium acetate solution or 0.4 M HCl, an average 99% Pd recovery has been reported. In this report the media in which the sorption occurred was not mentioned, though.

A two-step ion exchange method for the separation of base metals from Pt metals and the following separation of Rh from the rest of the Pt metals has been developed by Jiang Lingen *et al* [46]. This method is used for the recovery of Rh from Ni minerals and employs a NaCl solution. The distribution coefficients of the elements in different concentrations of NaCl at different pH values are also reported.

In HCl systems most of the Pt group metals are present as stable anionic chloro complexes and, hence, are retained by strong base anion exchange resins. The high selectivity shown by strongly basic anion exchange resins towards anionic chloro complexes of the Pd and Rh represents a favourable condition for their separation from associated base metals and many other elements. The most undesirable feature common to all methods utilizing this sorption principle, however, is that the elution of the Pt metals is complicated and not always complete. Incomplete recovery may also be the result of reduction of the metal ions to lower oxidation states or to the metals

while in contact with the resin. Furthermore, ion exchange separations are also affected by the manner in which the individual elements are dissolved and complications may also arise due to differences in behaviour between fresh and aged solutions caused by partial hydrolysis of the chloro complexes, especially in the case of Rh. Since all these negative effects may influence the determinations of Pt metal, usually only approximate distribution data are presented [25]. This may, nevertheless, serve as a guideline with respect to the interpretation and explanation of the empirical procedures presented here.

Ion exchange resins has been widely applied for separation of Cu in various samples. Both strongly basic anion exchange resins and cation exchange resins of the sulphonic acid type have been employed. Even at high concentrations of hydrochloric acid the distribution coefficients do not exceed a value of ~12, so that for the complete sorption of Cu from such systems relatively large ion exchange beds are required. To separate Cu from other more strongly sorbed elements such as Pd and Rh, Cu(II) can be eluted with 2 to 4 M HCl (K_d = 1 and ~4, respectively), while the co-sorbed elements are firmly retained by the resin.

In a study [31] on the separation of Pd from Rh, Pt and some other base metals (not including Cu), three anion exchange resins namely Amberlite IRA-68, IRA-93 (both weakly basic anion exchangers) and Amberlite IRA-400 (strongly basic anion exchanger) in their chloride forms have been used and compared. Palladium could be completely recovered from a 4 M hydrochloric acid solution containing 10 ml of a synthetic mixture of 250 ppm of each metal, by elution with different concentrations of ammonia. The Amberlite IRA-93 exhibits more favorable results in the elution of Pd.

4.2 EXPERIMENTAL

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4.2.1 Separation of Pd from Rh and Cu by the AG 50-X4 cation exchange resin

4.2.1.1 Reagents and equipment

The resin was purchased from Bio-Rad Laboratories, Richmond, California and instruments for the determination of natural elements and measuring the radioactivity are the same as described in chapter 2.

4.2.1.2 Separation procedure

A 5 cm × 1cm I.D. column was packed with the resin (200-400 mesh and H^+ form) and preconditioned with 25 ml 0.5 M HBr - 0.1 M thiourea solution. The solution containing the three elements (dissolved in 6M HCl) was evaporated to dryness, cooled down, dissolved in 25 ml 0.5 M HBr - 0.1 M thiourea solution and transferred to the column. The column was then washed with another 25 ml 0.5 M HBr-0.1 M thiourea solution for the elution of Rh followed by 25 ml distilled water. For the elution of Cu, 25 ml 2 M HCl and 25 ml 7 M HCl was used for the elution of Pd. The flow rate was 2 ml/min.

4.2.2 Distribution coefficients for Pd, Rh and Cu on the macroporous cation exchange resin AG MP-50 in HCl and the separation of Pd

4.2.2.1 Reagents and Equipment

The AG MP–50 macroreticular sulphonated polystyrene cation-exchanger (200-400 mesh, H^+ form) marketed by Bio-Rad Laboratories, Richmond, California, was used. All the other chemicals were of analytical grade.

4.2.2.2 Procedures

A- *Distribution Coefficient*

For purification of the resin, it was packed into a large column (20 cm × 3cm) and washed with 200 ml 5 M nitric acid solution, followed by distilled water. The method for the determination of distribution coefficients is described in the next section for IRA-93, except for the elution of the three elements 8 M hydrochloric acid was used (Table 4.3.1).

B - Separation of Pd

A 10 cm × 1cm I.D. column was packed with the resin and preconditioned with 25 ml 0.02 M HCl. ^{100}Pd was added to the sample for γ-spectrometry measurements. The sample was first evaporated to dryness, dissolved in 25 ml 0.02 M HCl and then transferred to the column with flow rate about 2 ml/min. Another 25 ml 0.02 M HCl was used to elute Rh. For elution of Cu, 25 ml ammonium acetate was used followed by 25 ml water. For elution of Pd 50 ml 7 M HCl was applied. To calculate the recovery of Pd one sample was taken from each step and measured by γ-spectrometry. Cu and Rh in the final solution were measured by ICP-OES technique.

4.2.3 Distribution coefficients for Pd, Rh and Cu on the weakly basic anion exchange resin Amberlite IRA-93 and separation of Pd

4.2.3.1 Reagents and equipment

The chemicals used were all of analytical grade. Copper solutions were prepared from its sulphate, palladium from its nitrate and rhodium as either metallic powder or $RhCl_3.3H_2O$. Rhodium powder was first dissolved in hot, concentrated sulphuric acid, evaporated to dryness, and then dissolved in 6 M hydrochloric acid. All stock solutions of the three elements were made up in 6 M HCl.

The Amberlite IRA-93 macroreticular polyamine functionality polystyrene (free base, 20 – 50 mesh) was purchased from Sigma-Aldrich (pty) Ltd. For converting the resin into chloride form, it was packed into a large column (20 cm × 3 cm) and washed with 200 ml 4 M hydrochloric acid followed by deionised water, obtained from a Milli-Q water purification system with 18 MΩ resistance.

4.2.3.2 Distribution coefficients

The cleaned resin was dried in an oven for 24 hours at about 90^0C. The dried resin was then weighed. The resin was put in the oven for another 2 hours and weighed again. The process was repeated until a constant mass was obtained to ensure the drying process was complete.

Distribution coefficients were determined by equilibrating 1.0 g of dry resin, in the chloride form, with 100 ml of solution over night (about 20 h) in a mechanical shaker. The solutions contained 0.05 millimole of each element. After equilibration, the resin was separated by filtration. For the elution of rhodium, 6 M hydrochloric acid was used, while copper and palladium required 2 M HCl and 5% ammonia solutions, respectively, to elute each element. The excess ammonia of the Pd eluate was gently evaporated and the acidity adjusted, by 10 M HCl, to a suitable concentration for

measurements. The amount of element in the aqueous and resin phases was determined by the ICP-AES technique.

4.2.4 AG 1-X8 anion exchange resin using HNO_3

4.2.4.1 Reagents and equipment

The reagents and equipment are the same as described in the previous chapters.

4.2.4.2 Procedure

A 12 cm × 0.8 cm I.D. column was packed with the resin which was converted to the nitrate form by passing 3 M HNO_3 through the column until the eluate contained no chloride. The resin was finally equilibrated with 50 ml 3 M HNO_3. The solution containing Rh and Pd in nitric was prepared as follows: A 280 mg tablet of $RhCl_3.xH_2O$ was first dissolved in 1 M NaOH solution under heating. After the formation of yellow hydrated rhodium oxide, $Rh_2O_3.xH_2O$ [19], 15 ml of 3 M nitric acid were added to dissolve the precipitate. The amount of Pd used in these synthetic samples was about 1 mg. The solution was then pumped through the column with a peristaltic pump at a flow rate of 1.8 ml/min. Rh was eluted washed with 50 ml 3 M HNO_3 and Pd with 50 ml water followed by 100 ml 5% ammonia solution.

4.2.5 Carrier-free ^{103}Pd separation from Rh targets by AG1-X8 anion exchange resin

4.2.5.1 Reagents and equipment

Anion exchange resin AG1–X8 (Cl^- form and 100 – 200 mesh) was purchased from Bio–Rad Laboratories (Richmond, California) and $RhCl_3.xH_2O$ was supplied by STREM Chemical Inc. (Newburyport, MA) and used as the target material.

The instruments for measurements of natural elements and radioactivity are described in chapter 3.

4.2.5.2 Ion exchange separation

The Rh chloride target was prepared by pressing $RhCl_3.xH_2O$ (140 mg) into thin 79 mg/cm^2 tablets (15 mm diameter) using a set-and-die tool operated at 2 Mpa (20 bar). A column (5 cm × 1cm) was packed with the resin and preconditioned with 25 ml 6 M hydrochloric acid solution. The flow rate of the solutions was 1.7 –1.8 ml/min controlled by a peristaltic pump. The 66 MeV proton bombarded target was dissolved in 20 ml hot 6 M HCl. The solution was cooled down to room temperature and then filtered, using a 0.45 μ Millipore filter, to remove any undissolved material (most probably rhodium oxide). The filtrate was pumped through the column from the bottom to the top. Rh was eluted with 35 ml 6 M hydrochloric acid, followed by 25 ml of distilled water to remove the acid and, finally, 50 ml 5% ammonia solution to elute the palladium from the column.

For measurement of natural elements involved in the study, an ICP-atomic emission spectrophotometer Perkin-Elmer P400 was used.

4.3 RESULTS AND DISCUSSION

4.3.1 Separation of Pd from Rh and Cu by AG 50-X4 cation exchange resin

Strong sorption of Pd on strongly acidic cation exchange resins such as Dowex 50 occurs if the dilute HCl or HBr media used contain thiourea in molar concentrations of 0.1 or 0.2. Rh is less strongly sorbed on the cationic rsins, for example, in 0.5 M HCl - 0.1 M thiourea Pd and Rh have distribution coefficients of >1000 and ~50, respectively [25]. This is due to the fact that thiourea forms moderately to very stable complexes with all Pt group metals , including Rh(III) and Pd(II). The formation of thiourea complexes and any subsequent exchange of ligands may also take place at rates that can vary considerably, thus, while the formation of cationic thiourea complexes is rapid for Pd, it is very slow in the case of Rh(III) [25,32,33]. These differences in ligand exchange rare and the fact that chloro complexes of Pd are stronger than the bromo complexes were exploited for the separation. Thus, the HBr - thiourea system, 0.5 M HBr - 0.1 M thiourea solution, was investigated for the separation of Pd from Rh and Cu. The column size was 10 cm × 1 cm I.D. and the amount of Rh, Cu and Pd used was 10 mg, 100 mg and ~10 μg, respectively. ^{100}Pd was used as a tracer (obtained from bombarding a Ag target). The flow rate was set at about 2 ml/min. For the elution of Cu, 2 M HCl solution was used (Rh was not sorbed under this condition), while for the elution of Pd, 7 M HCl was employed. The volume of solution used in each step was 50 ml. A recovery of 92.8 ± 5.6% was obtained for Pd. Rh and Cu in the final solution was found to be less than the detection limit of the ICP instrument.

Thiourea solutions almost always contain small amounts of finely dispersed S (sulphur). This and any additional S formed in the presence of various oxidising agents, does not present serious problems in separations involving the thio-compound. When an impervious S layer forms at the top of a resin column and impedes the flow of the eluent, it can simply be broken up with the tip of a glass rod (which is not

possible in a hot cell). Pd in the final solution is probably present as the thiourea complex ($Pd(tu)_2^{2+}$). For any further processing for production of "seeds", the thiourea should be destroyed and this process is usually achieved at high temperatures [25] and at high temperatures Pd in the compound is reduced to the metallic form [26].

The advantage of this procedure is that by using one single column, while separating Pd, at the same time the precious Rh is also recovered and can be re-used for the targetry. Whether the presence of thiourea may interfere with the separation or ^{103}Pd seed preparation, still needs to be investigated later.

4.3.2 Strongly acidic cation exchange resins for separation of Pd and determination of distribution coefficients for Pd, Rh and Cu on the macroporous cation exchange resin AG MP-50 in HCl

The distribution coefficients for these elements in pure aqueous solutions on some strongly acidic cation exchange resins, including the macroreticular resin AG MP-50, have already been reported in which the values for Pd and Rh in all concentrations of HCl, 0.1 M and larger, do not exceed 4.2 [25,48]. Considering these results, in early experiments attempts were made to use a cation exchange resin for the isolation of Cu from Pd and Rh in dilute hydrochloric acid. It was expected that only Cu would be retained and the Pd and Rh would pass through the resin. Pd could subsequently be separated from Rh by using an anion exchange resin (see Section 4.3.3). In this way the pure recovered Rh is re-useable for further target preparations.

In practice, however, when a synthetic solution containing micrograms of Pd (*ca.*100 micrograms) with milligrams of Cu and Rh was used, it was found that even in 0.5 M HCl a large portion of the Pd (up to 60%) was sorbed on a 10 cm column packed with cation exchange resins whereas the Rh was not retained. The sorption of Pd, showed similar characteristics with the three cation exchange resins AG 50W-X4, AG 50W-X8, and macroporous AG MP-50. For the elution of Pd from the resins 8 M

HCl or 8 M HBr were required. The elution was more efficient on the AG MP-50 resin (wide infra) and it was decided to repeat the determination of the distribution coefficients on this resin. The results are shown in Table 4.3.1.

Table 4.3.1 Distribution coefficients for Pd, Rh and Cu on the macroporous cation exchange resin AG MP-50 in HCl.

Element	M HCl			
	0.1	**0.2**	**0.5**	**1.0**
Rh	9.8	9.0	8.4	8.0
Pd	10.0	10.0	10.0	7.6
Cu	1620	446	100	30.3

The distribution coefficients using cation exchange resins generally decrease with increasing acid concentration from 0.1 to 1.0 M HCl [48]. The present results differ from published values. For both Pd and Rh the distribution coefficients are a little higher (Section 4.3.2). This can be due to the original reagents, the way of preparation (see for example, Section 4.1.2.2. on the ion exchange behaviour of Rh) and, to some extent, to the technique of measurement. In this work the solutions were prepared from $RhCl_3.3H_2O$, $Pd(NO_3)_2$, and $CuSO_4.5H_2O$. These distribution coefficient values, however, especially for Pd, are still too small to explain the strong

sorption on the cation exchange resins indicating that when working with trace amount of elements, the distribution coefficient data, which most of the time are obtained from rather high concentration of elements (for an exception compare reference 29), are not necessarily a complete criteria for ion exchange separation. Other important differences between the conditions of the practical separation and distribution coefficient determination are the methods used: column versus batch, and the amount of resin, which is usually more in the column separation. Nevertheless, for complete sorption of Pd on the various cation exchange resins, a series of experiments were conducted in more dilute HCl medium (0.02 M). The results are summarised in Table 4.3.2. In these experiments ^{100} Pd was added to the sample as a tracer. Measuring the ^{100} Pd in the effluents, quantitative retention of Pd by all the three resins were indicated. The results show that the best recovery (> 90%) was obtained using the AG MP-50 resin.

Table 4.3.2 Cation exchange resins for separation of Pd from Rh and Cu in 0.02 M HCl.

Resin	**Recovery of Pd**	**Eluent**
AG 50-X4	65.8%	8 M HCl, 50 ml
AG 50-X8	81.2%	8 M HCl, 50 ml
AG MP-50	92.1%	8 M HCl, 50 ml
AG MP-50	90.1%	8 M HBr, 25ml

4.3.3 Distribution coefficients for Pd, Rh and Cu on the weakly basic anion exchange resin Amberlite IRA-93

Although Amberlite IRA-93 had been used for recovery of Pt metals from some base metals in automotive catalytic converters [31], the procedure was also very well suited for our endeavour: the separation of Pd from Cu and Rh. The dissolved target only needed to be diluted to 4 M HCl. To obtain the optimum acid concentration, the determination of distribution coefficients were conducted in six different HCl concentrations.

For each chosen concentration of HCl, three samples were prepared and placed together with the other samples on a mechanical shaker. For Pd, for example, in total 18 samples of six concentrations were prepared and shaken together. Both filtrate and eluate (see procedure, Section 4.2.3) were diluted to 250 ml 2 M HCl. In this way the error from matrix effects was minimised. Since the response of the ICP instrument was different from day to day, all the solutions were analysed simultaneously and compared with the analysis of the original solution (0.05 millimole of each element in 250 ml 2 M HCl). Distribution coefficients were calculated with the usual equation:

$$K_d = \frac{[(\text{mass of element sorbed on resin}) \times (\text{volume of solution, ml})]}{[(\text{mass of element in solution}) \times (\text{mass of dry resin, g})]} = [(C_0 - C) \times v] / [C \times m],$$

where C_0 and C are the concentrations of the original and equilibrated solution respectively, v is the volume (ml) of the solution mixed with dry resin (100 ml) and m is the mass (g) of dry resin (1 g).

Table 4.3.3. shows the distribution coefficients for the three elements at six different hydrochloric acid concentrations. The K_d values are averages of the three samples of each concentration. For copper, as expected, the K_d's decrease with decreasing concentration of HCl and in 0.5 and 1 M HCl it was not even retained on the resin.

Table 4.3.3. Distribution coefficients for Pd, Rh, and Cu on the weakly basic anion exchange Amberlite IRA-93 resin in HCl media.

	M HCl					
Element	**0.5**	**1.0**	**2.0**	**3.0**	**4.0**	**6.0**
Pd	1225	1021	792	510	393	22
Rh	135	118	33	25	21	18
Cu	-	-	1.1	3.4	10.4	32

The first objective for using this resin was to separate Pd from Rh after separating Cu initially on a cation exchange resin. In this way Rh could be recovered free from copper and re-used as target material. The size of the column was 12 cm × 0.8 I.D.cm and 4 M HCl solution was chosen as the medium for the sorption of Pd. Solutions were transferred to the column using a peristaltic pump at a flow rate of 1 ml/min. All Pd and some of the Rh and Cu were sorbed. The Rh was then eluted using 6 M HCl, Cu with 2 M HCl and finally, Pd using 5% ammonia solution.

Several experiments were performed using three different flow rates. The yields of recovery of Pd were 78.3 (average of 3 experiments), 86.0 ± 5.0% (7 experiments), and 94.7% (average of 3 experiments) with flow rates of 3, 2, and 1 ml/min respectively. The amounts of Rh and Cu in the final solutions were less than the detection limit of the ICP instrument (Varian P400). The original solutions contained approximately 500 μg of Pd, 10 mg Rh, and 20 mg Cu. The recovery yield is somewhat less than that reported previously (100%) [31] attributable to both the

length of the column and the lower quantity of Pd used here. Indeed, when the experiment was repeated in a carrier-free separation, with about 10 μg natural palladium and ^{100}Pd (as tracer), the recovery was less than 20%, even by increasing the volume of ammonia solution to 200 ml. As can be seen from Table 4.3.3, 3 M hydrochloric acid is even more suitable for the separation of Pd from Rh and Cu.

The second important and novel reason for developing this method, was to use this resin as a substitute for graphite pellets (see Chapter 1, Fig. 1.2.2.) in order to load the ^{103}Pd activity on to it and to be used in Ti tubes as "seeds". This very hard resin has a rather spherical shape and is suitable for this purpose. In fact, even before the above results were available, a number of experiments in the same acid concentration, mentioned above, were carried out to load Pd on small amounts of the resin. In these experiments, utilising 150 mg of resin and a solution containing only Pd (ca. 1 mg), the solution was countercurrently re-circulated through the column continuously using a peristaltic pump. After four hours of circulation, the pump was stopped and the solution analysed for Pd. These results were promising showing that about 90% of the Pd was sorbed by the resin. Of course, with the distribution coefficients known, this process using 0.5 M HCl can be applied more efficiently (Chapter 5).

4.3.4 AG 1-X8 anion exchange resin for the separation of Pd from Rh using HNO_3

Nitric acid was also investigated for this separation because this media was used for the separation of Pd from Ag and Rh (see also Chapter 2). The experiments were achieved using natural elements (and ICP analysis). In each experiment a new resin column was used. Since the chloro complexes of Rh are very stable and inert [32,33], direct dissolution by nitric acid was avoided (Section 4.2.4). Thus Rh was first converted to aquo then treated with HNO_3. Although quantitative retention of Pd was obtained, only 67.3 ± 11.9% recovery was found on elution and the concentration of Rh in the final solution (50 ml) was 2.8 ± 1.6 ppm (from 280 mg $RhCl_3.3H_2O$). The

low recovery, indicating incomplete elution, and the high error showed that the procedure was not reproducible and reliable (see also Chapter 2, Section 2.3.3).

4.3.5 Carrier-free ^{103}Pd separation from Rh targets using AG1-X8 anion exchange resin

All radionuclides for medical purposes, that is for diagnosis, therapy and labelling, must be carrier-free because they are, in their special radiochemical form, collected in certain tissues of interest. Although for seed implantation in brachytherapy carriers do not play very important roles, a carrier–free separation would be preferred and more desirable. For the production of ^{103}Pd-seeds with high activity per seed, obtaining a high specific activity from the radiochemical separation is advantageous, especially, when the seeds are not to be used immediately. Indeed, as discussed in Section 4.3.3, the weakly basic anion exchange resin Amberlite IRA-93 was successfully used for the separation of carrier-added Pd from Rh and Cu (low concentrations).

On strongly basic anion exchange resins Pd(II) is sorbed from HCl solutions with concentrations ranging from ca. 0.1 to 12 M. The species retained by the resin (forming a dark red band) is $PdCl_6^{4-}$, which in 2 to 12 M HCl solutions is also the predominant complex present [25]. In 0.5 to 2.0 M acid the complex $PdCl_4^{2-}$ prevails. The sorption of Pd on AG1-X8 is higher by about two orders of magnitude than that of Rh(III) and decreases with increasing concentration of HCl. Nevertheless, the distribution coefficients of Pd(II) in the range of HCl concentrations from 0.1 to 12 M (Kd > 10^3 to ca. 40, respectively) are sufficiently high to allow this element to be separated from Rh [25]. In 6 to 12 M HCl media, divalent Cu forms anionic chloro complexes, i.e. $CuCl_3^-$ and also $CuCl_4^{2-}$, which are weakly retained by strongly basic anion exchange resins such as Dowex 1. At lower HCl concentrations, (4 to 6, 2 to 4, and 0.1 to 2.0 M), the Cu is present as $CuCl_2$ and the hydrated species, $CuCl^+$(aq) and Cu^{2+}(aq), respectively [25]. This complexation is in line with essentially nonsorbability of Cu(II) from 0.1 to 6 M HCl solutions as shown by distribution coefficients of less than unity.

For the elution of Rh, 6 M HCl (Kd = ~1) and for Pd - sorbed as $PdCl_6^{4-}$ - 12 M HCl can be used; under which condition its distribution coefficient is low enough (ca. 40). It can be effectively eluted by 1 M ammonia solution [25].

In the light of the above-mentioned ion exchange behaviour of the elements, the strongly basic anion exchanger AG1-X8 in a 6 M HCl medium was chosen for the separation. After testing the procedure using natural elements, the process was repeated with radionuclides of the elements (Pd and Rh). For the production of ^{103}Pd from Rh, a 15 mm-diameter rhodium chloride tablet was employed as the target. On bombardment of the target with a 66 MeV proton beam, in addition to ^{103}Pd (21 keV), the other isotopes of Pd such as ^{100}Pd (84 and 126 keV), isotopes of Rh (e.g. ^{101m}Rh, 306.9 keV), isotopes of Ru (e.g. ^{97}Ru, 215.7 keV), and isotopes of Tc (e.g. ^{95}Tc, 756.8 keV) were produced in the Rh target (see also Section 4.4). The γ-lines of the isotopes with largest branching ratio and longest half-life were used for γ-spectrometry to evaluate the efficiency of the radiochemical separation. The results of the γ-spectrometry showed that Pd and Tc were quantitatively retained by the resin, while Ru quantitatively and more than 99.8% of Rh was eluted by the 6 M HCl. However, when 25 ml water, followed by 50 ml 5% ammonia solution was used for the elution of Pd an average recovery of 92% was obtained. On elution of Pd, Tc was still retained on the resin. When this procedure was also used for the isolation of Rh isotopes from the rest of the isotopes produced on bombardment of Rh by 400 MeV ^{16}O and ^{12}C, the retention of Ru was required. Since Ru(IV) and Pd have the same distribution coefficient in 6 M HCl [25], this result showed that only Ru(III) was formed on dissolution of the target. Ru(III), in the presence of H_2O_2, was then oxidised to Ru(IV) which was subsequently quantitatively retained by the resin. No attempt was made to evaporate the excess H_2O_2, which was necessary to keep Ru in the oxidised form, and although there were bubbles in the solution during the pumping, it did not cause any problem during the process. It should be noted that for commercial production of ^{103}Pd from a Rh target, the target is bombarded with ca. 22 MeV proton beam (see Chapter 1, Section 1.3) and neither Tc nor Ru would be produced.

No attempt was made to measure the natural Rh in final radioactive solutions but in a radionuclide production for medical purposes, the final solution is always analyzed for radionuclide as well as chemical impurities (see also Chapter 1, Section 1.4). In the experiment, repeated several times with natural Rh and Cu (as the potential substrate of electroplated Rh), Rh and Cu concentrations in the final solution were measured by ICP-OES technique. The results of these measurements revealed that concentration of Rh was 1.6 ppm in the 50 ml final solution, while the Cu concentration was less than the detection limit of the instrument.

4.4 CONCLUSIONS

4.4.1 Carrier-free ^{103}Pd separation from Rh targets using the anion exchange resin AG1-X8

From the five ion exchange chromatographic procedures investigated for the separation of Pd from Rh and Cu, two were developed successfully for the separation of carrier-free ^{103}Pd – the cation exchange resin AG 50-X4 (Section 4.3.1) and AG 1-X8 anion exchange resin (Section 4.3.5). Using the AG 50-X4 resin, the advantage is that Rh is recovered directly and the disadvantages are that the original solution obtained by dissolving the target must first be evaporated and problems associated with presence of thiourea (as discussed in Section 4.3.1). Using AG 1-X8 anion exchange resin, in contrast, necessitates no evaporation of the original solution and the acidity of the final solution can be adjusted readily for seed preparation. Furthermore, because the second procedure allows the separation of Rh from Pd, Tc and Ru, it can be used for other applications in which Rh targets are involved [24,39]. As an example, ^{101m}Rh is one of the Rh radioisotopes that has desirable nuclear characteristics and a potential radionuclide for use in nuclear medicine. Carrier-free separation of ^{101}Pd for production of ^{101m}Rh is, therefore, essential. There is some information about excitation functions in the range of 66 → 15 MeV for direct production of ^{101m}Rh via the ^{103}Rh (p,3n) ^{101}Pd → ^{101m}Rh reaction. The chemical procedure, therefore, is able to separate the ^{101}Pd (parent of ^{101m}Rh) selectively from the isotopes of Rh, Tc, and Ru produced during the bombardment.

A combination of a Rh target and a Ag target can be used to substantially reduce the ^{100}Pd impurity (from the Ag target, Section 2.3). A silver target can be bombarded with proton in the 66 → 0 Mev energy window and set aside for a week. The second week a second silver target is bombarded (in the 66 → 24 MeV energy window) in tandem with a rhodium target (in 22 → 0 MeV energy window). The second Ag target is set aside for a week and the first Ag target and the Rh target are then processed to

recover ^{103}Pd. The final products obtained from the two targets are combined to obtain a ^{103}Pd product containing <1% ^{100}Pd with a total yield of ca. 24 MBq/μAh.

CHAPTER 5

PREPARATION OF THE SEEDS FOR BRACHYTHERAPY

5.1 INTRODUCTION

One of the ^{103}Pd seed models, which has been exclusively used in recent years, (Chapter 1, Section 1.2.6.3, Fig. 1.2.2) consists of two rectangular Pd-plated graphite pellets separated by a rectangular lead X-ray marker (1.0 mm × 0.5mm) [6,7]. The dimensions of the pellets are 0.9 mm × 0.6 mm. Considering the 0.7 mm inner diameter of the titanium tube, the thickness of each graphite pellet must be 0.3 mm or less to be able to move easily through the tube.

Electroplated palladium (and other Pt metals) on graphite are most frequently used as catalyst for hydrogenation of organic molecules. In one study Polcaro *et al.* have investigated the electroplating of Pd on carbon felt (as a catalyst support) [49]. The electrochemical performance of carbon felt electrodes (made of thin fibres about 10 μm thick) with Pd has been examined by cyclic voltammetry. These studies, in 0.1 M hydrochloric acid media, indicate that with rather high concentrations of Pd (ca. 5×10^{-3}M), H_3O^+ reduction takes place as well. Although no details are provided, it is claimed that an NH_4Cl-NH_3 solution can be used for the electroplating of ^{103}Pd on graphite for brachytherapy [9].

5.2 EXPERIMENTAL

5.2.1 Equipment and material

The Ti tubes machined from titanium rods (4.5 mm length, I.D = 0.7 mm and O.D = 0.8 mm) were purchased from Wagner System Co. (Diep River, South Africa). Thin Ti foils with thicknesses of 0.02 mm and 0.05 mm (supplied by Goodfellow Cambridge Ltd., Cambridge, England) were used as caps for the tubes.

To seal the tubes, a spot-welding machine UNITEK 250 with a UNITEK heavy-duty welding head Model 37 (UNITEK Corporation Equipment Division, Monrovio, California, U.S.A) was utilised for the welding of the caps to the tubes.
The analytical grade macroreticular weakly basic anion exchange resin Amberlite IRA-93 was used for sorption of the final ^{103}Pd product.

5.2.2 Procedures

5.2.2.1 Electroplating of ^{103}Pd on graphite sheet

A 25 ml solution of 5×10^{-3} M Pd(II) in 0.1 M HCl was used as the bath. ^{103}Pd was added to the solution as a tracer, the cathode was a circular sheet of graphite (with 2 cm diameter and 0.5 mm thickness), a Pt wire as the anode with a current of 15 mA. Every 10 minutes a 100 μL sample was taken from the electrolysis bath and the Pd content was measured (100 seconds) with the X-ray detector (described in Chapter 2).

5.2.2.2 Sorption of ^{103}Pd on the resin

The final solution from the radiochemical separation was first evaporated gently to about 1 ml. Acidity of this solution was then adjusted to 0.5 M HCl by addition of concentrated HCl and water to a total volume of 20 ml. While stirring, the solution

was re-circled through a column packed with 150 mg of the resin (flow rate 2-3 ml/min, at room temperature) from the bottom to the top. The process was continued for 2 hours. The resin was then washed with distilled water and dried by pumping air through the column (ca. 5 min.).

5.2.2.3 Determination of the distribution of ^{103}Pd on the resin beads

The procedure was the same as described in previous section except that the sample contained 1mg natural Pd and ^{103}Pd was added as the tracer. After the sorption of the Pd on to the resin, the dried resin beads were mixed well and 10 resin beads were placed into a conic polypropylene vial (Corning Incorporated, Corning, NY 14831). Each vial was then placed on the X-ray detector and counted for 100 seconds. The 20.1 keV signal was used as the ^{103}Pd peak.

5.2.2.4 Enclosing the Ti tubes by welding

Each Ti tube - already closed at one end - was filled with 6 resin beads using a funnel. The open end of the tube was then closed by welding the cap on to the tube. The caps of the tubes were punched by a matrix (0.8 mm diameter) and a rounded pierce so that the cap had a hemispherical shape. The welding was achieved as follows: The Ti tube, together with its holder was put into the lower electrode and clamped, followed by placing the cap on the top. The upper electrode was brought in touch with the cap and the electric pulse was discharged. Other instrument settings used were:

Pulse = 1

Polarity = reverse

Manual heat = 5 watt seconds

5.3 RESULTS AND DISCUSSION

This is the most important and challenging part of this work for several reasons: Firstly, since the number of resin beads for the sorption of certain amounts of ^{103}Pd produced are limited (at least 2 mCi ^{103}Pd on a maximum of 6 resin beads in one Ti tube), conventional ion exchange chromatography techniques are not as effective for this purpose. A technique, therefore, has to be developed for the sorption of ^{103}Pd on a certain number of the resin beads. Secondly, because of the very thin walls of the Ti tube (0.05 mm) and the caps (for sealing the tubes), great care must be taken not to squash the tubes. The spot-welding machine is also to be operated manually and mechanically, adding to the sensitivity of the process. In addition, designing necessary parts, for transferring the resin beads into the Ti tubes, holding the tubes in the welding machine and alterations on the machine in order to easily facilitate such a delicate welding, are discussed in this section.

5.3.1 Electroplating of ^{103}Pd on graphite sheet

An experiment was conducted using the first procedure mentioned above (Section 5.1, [49]). To obtain an electrolyte bath free from nitrate ions, which could effect the quality of the plating, the mixed solution of natural Pd and ^{103}Pd was first evaporated, the residue dissolved in concentrated HCl, evaporated again and finally dissolved in 0.1 M HCl. The results are presented in Fig. 5.3.1. It can be seen that after about two hours electroplating the concentration of Pd in the bath had decreased to less than 5% of the original.

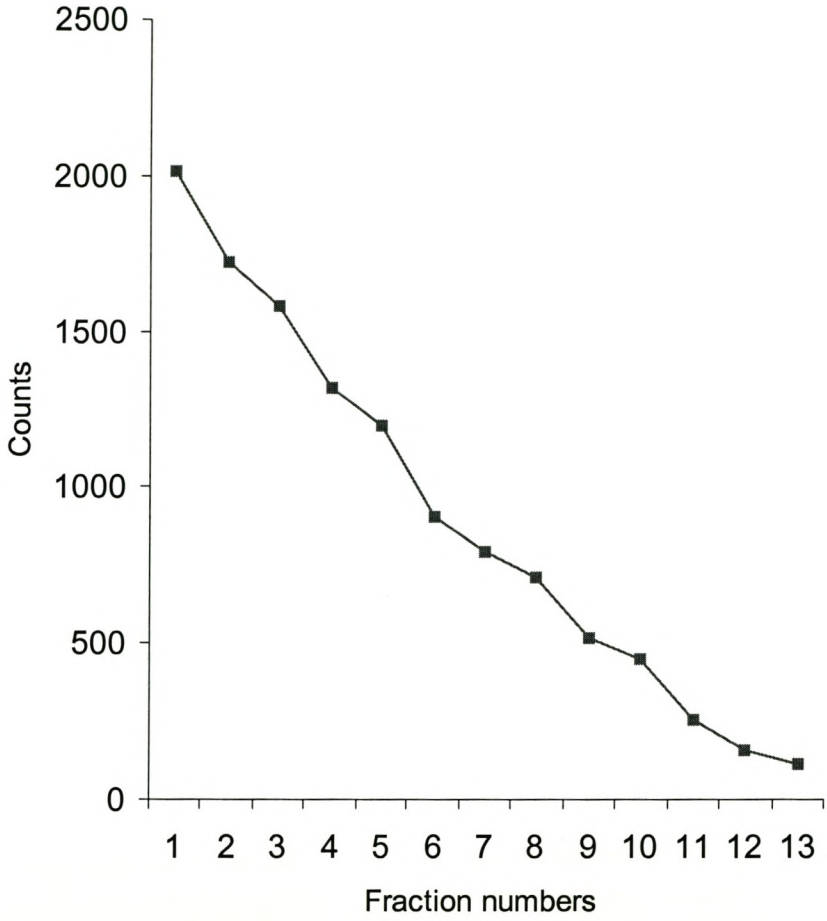


Fig. 5.3.1 Electroplating of ^{103}Pd on graphite sheet (electrolyte: 5×10^{-3} M Pd(II) in 0.1 M HCl).

5.3.2 Sorption of Pd-103 on Amberlite IRA-93 resin

Cutting the ^{103}Pd electroplated graphite into such small pieces (Section 5.1), however, was found to be extremely difficult. An ion exchange resin was, therefore, considered

as alternative carrier in the seed preparation. Since the Amberlite IRA-93 anion exchange resin was already available and had been used for some separation experiments, it was selected for the sorption of ^{103}Pd. Having a spherical shape, the resin beads are very well suited for the easy transfer of the activity into the Ti tubes. The 20-50 mesh (300-850 μ) resin purchased in free base form, was first converted to chloride form by treating with HCl. This conversion was necessary before the final process because it leads to a 5% increase in volume of the resin beads (Fluka, catalogue 1999-2000). A column method was employed for the conversion using 4 M HCl solution. The resin was subsequently washed with deionised water, dried and then screened using two sieves (with 600 and 700 μ apertures) to pick out the suitable size to move through the Ti tube. Approximately 140-150 mg of the resin was packed in a 0.5 cm (I.D.) × 1cm column. Even before the determination of the distribution coefficients of Pd on this resin was achieved, four experiments were performed using 4 M HCl. These experiments indicated that after 4 hours of recycling a solution of Pd through the column, an average of 90% Pd was sorbed by the resin. In 0.5 M HCl, the same result was obtained within 2 hours.

5.3.3 Distribution of ^{103}Pd on the resin beads

The even distribution of activity between the seeds is essential. In a typical brachytherapy treatment, the medical physicist having measured the size and shape of the gland and the aggressiveness of the cancer calculates the needed activity and thus how many seeds are required for the particular case. These are based on the assumption that the activities of seeds are similar. In this work, therefore, uniform distribution of activity on resin beads had to be ascertained and determined.

The average count of 80 samples was 200217 with a relative standard deviation of 5.7% indicating an even distribution.

5.3.4 Transferring the activity-loaded resin beads into the Ti tubes

For transferring the beads into the Ti tubes, a small copper funnel was designed and made. The bottom diameter of the funnel was 0.9 mm (0.1 mm larger than the outer diameter of the tube, Fig. 5.3.2) contained a chamfer to fit easily over the Ti tube.

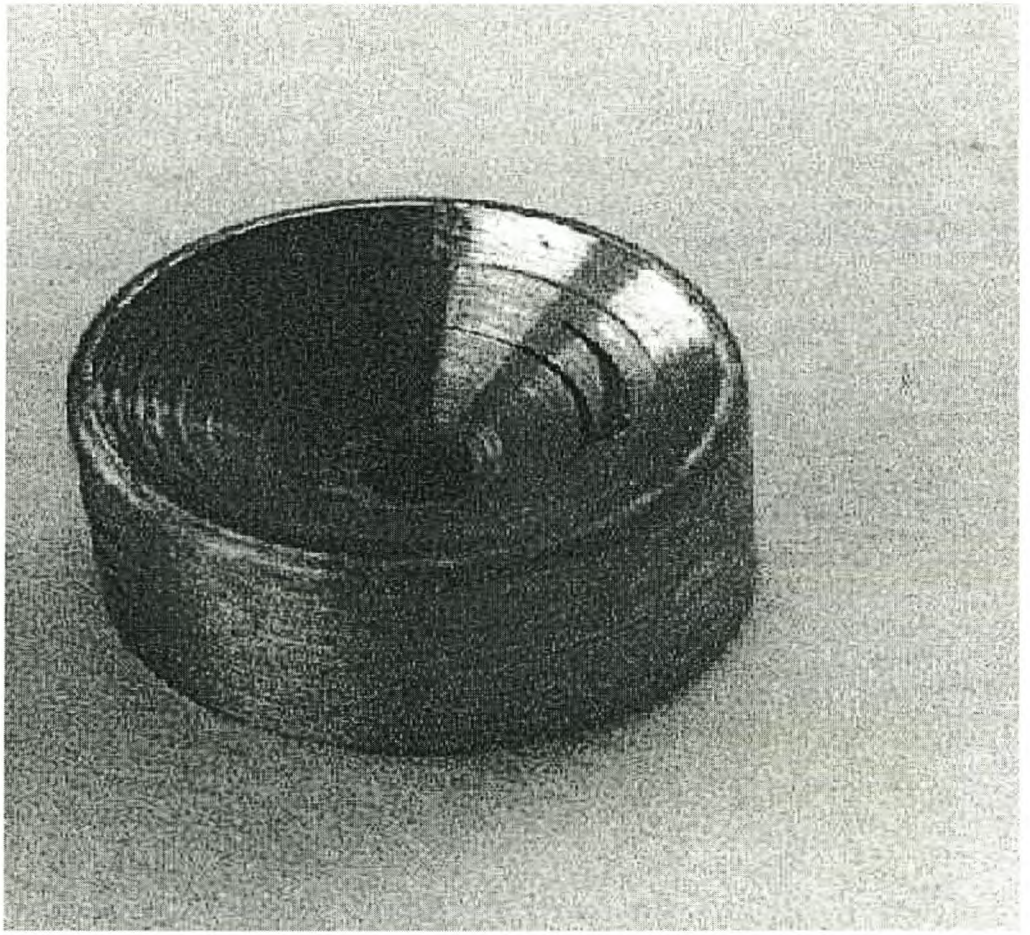


Fig. 5.3.2 The copper funnel to transfer the resin beads into the Ti tubes.

5.3.5 Enclosing the Ti tubes by using a spot-welding machine

Commercial seed manufacturers usually use electron beam or laser beam instruments to close the Ti tubes after filling it with the radioactivity (Chapter 1). For this, two small cylindrical titanium cups are put into the two ends of the tube, and as the tube is turned around, the welding is achieved. A typical electron beam machine of the kind cost more than USD 500000.

Due to the lack of such expensive equipment at iThemba LABS, attempts were first made to seal the tubes by crimping the two ends. For this purpose a 4-jar piece was designed and machined. Each jar was a 90-degree 3D arc. The four jars were welded together at one end to which a screw-thread was machined. The tube was held in a hole made in a copper cylinder so that 0.5 mm of the tube was exposed to be pressed (Fig. 5.3.3). This cylinder, together with the tube, was put in the centre of another cylinder through which the jar system could move up and down. By moving the jar system down over the tube and screwing it, the tube was crimped. Fig. 5.3.3 illustrates the different pieces of this device.

Despite the expected symmetrical crimping, the tube had a tendency to be squashed in 3 directions, resulting in a " T " shape so that the crimped part became wider than the original diameter of the tube (i.e. > 0.8 mm). Therefore, it was impossible to place the tube inside the tube holder for crimping of the other side. No improvement was observed when two different crimping devices, with 6 and 8 jars, were used. Welding was, therefore, considered a better option for sealing the tubes.

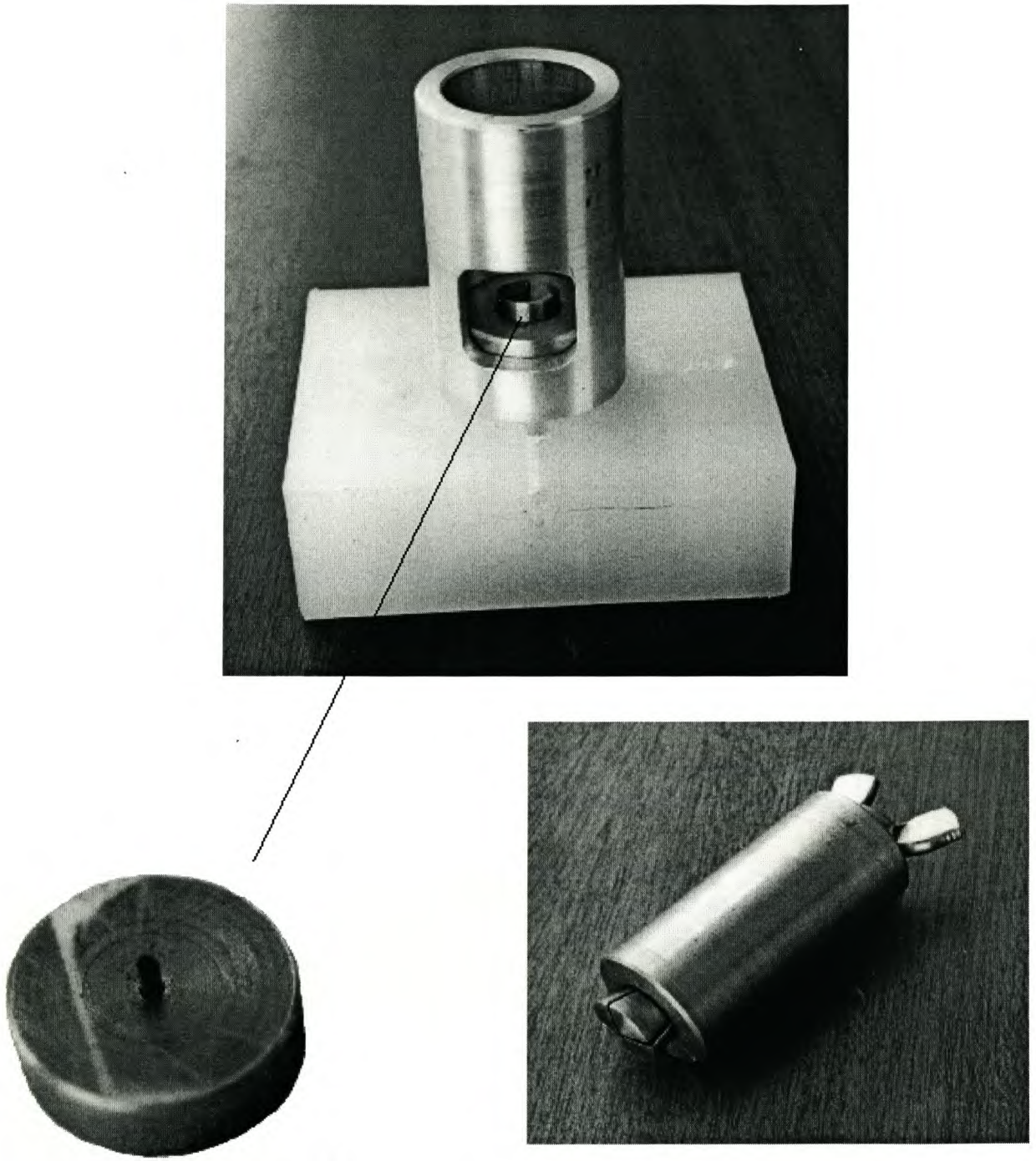


Fig. 5.3.3. The devices designed for crimping the Ti tubes.

Fig. 5.3.4 and Fig. 5.3.5 show the spot-welding machine available at iThemba LABS. The welding is based on heat generated by an electric pulse between two electrodes. To control the heat, the machine can be operated in two modes: preset (buttons 1-5) and manual (button M), from 0 to 250 watt seconds. The pedal is used to move the upper electrode to the lower electrode. When the two electrodes touch, moving the pedal a little more a strong spring (in the welding head and over the upper electrode) is pressed activating a micro switch, followed by an electric pulse between the electrodes. We first tested the machine for welding thin Ti foils (0.02 mm and 0.05 mm thick). After obtaining strong welding the different parts, including the tube holder, two electrodes, and clamping were designed and machined. Fig. 5.3.6 illustrates all the parts. The clamp was used to hold the tube, tube holder and lower electrode together to ensure electric contact between them. The diameter of the upper electrode at the tip was 0.8 mm. The caps of the tubes, essential for sealing, are shown in Fig. 5.3.7.

As mentioned above, the electric discharge only occurred if pressure on the two electrodes was sufficiently high to press together the strong spring. This pressure was too high and it smashed the tube when welding. The micro switch, therefore, was removed from its original position so that it can be activated by pushing a button (the small one on the welding head).

The quality of the welding was monitored under a microscope. The photomicrographs in Figs. 5.3.8 and 5.3.9 show side and top views of the welding. The appearance of the welding indicates successful welding. Using ready-made Ti tubes and having the caps machined, even a better quality and appearance of the welding will be obtained.

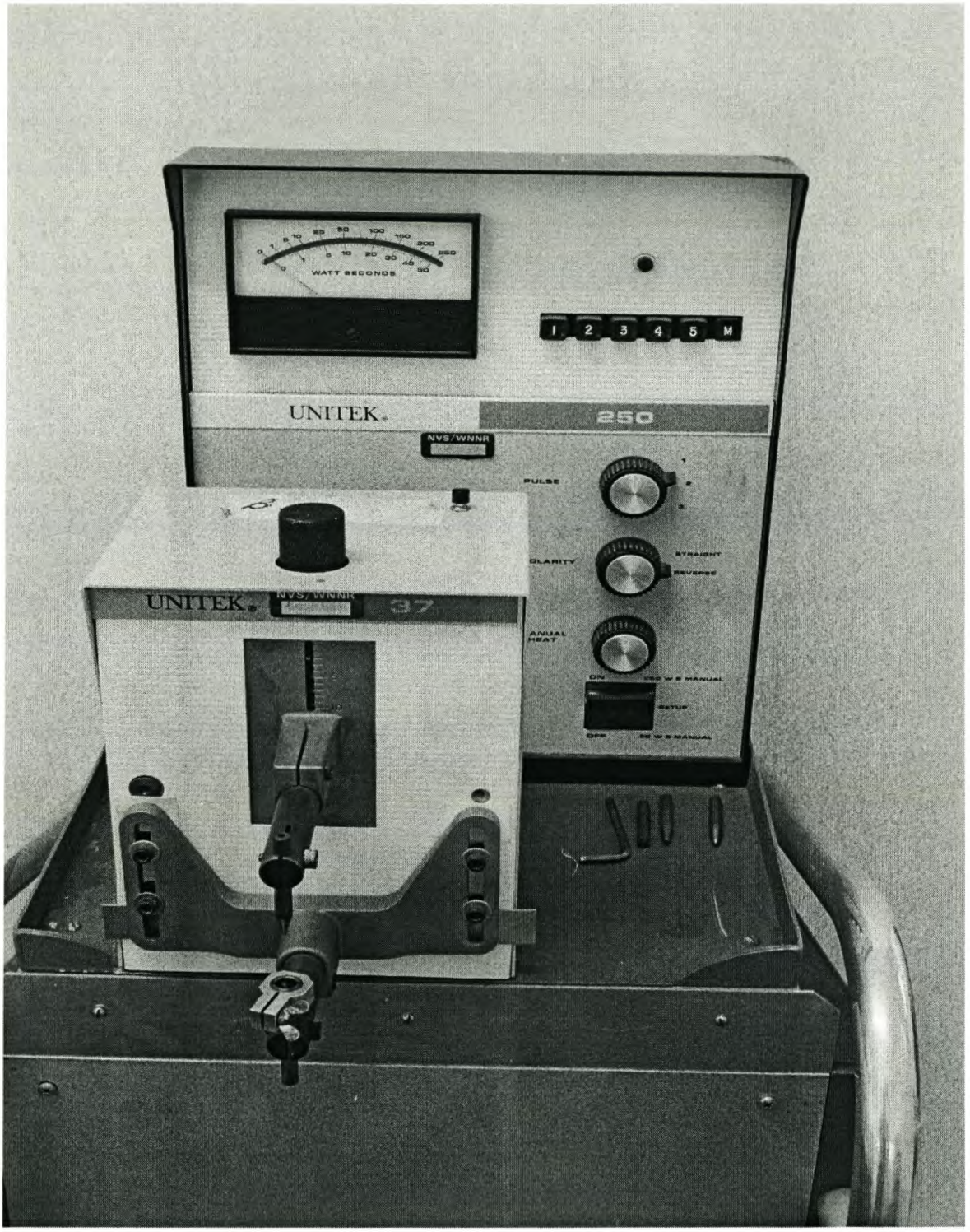


Fig. 5.3. 4 The spot-welding machine (top section).

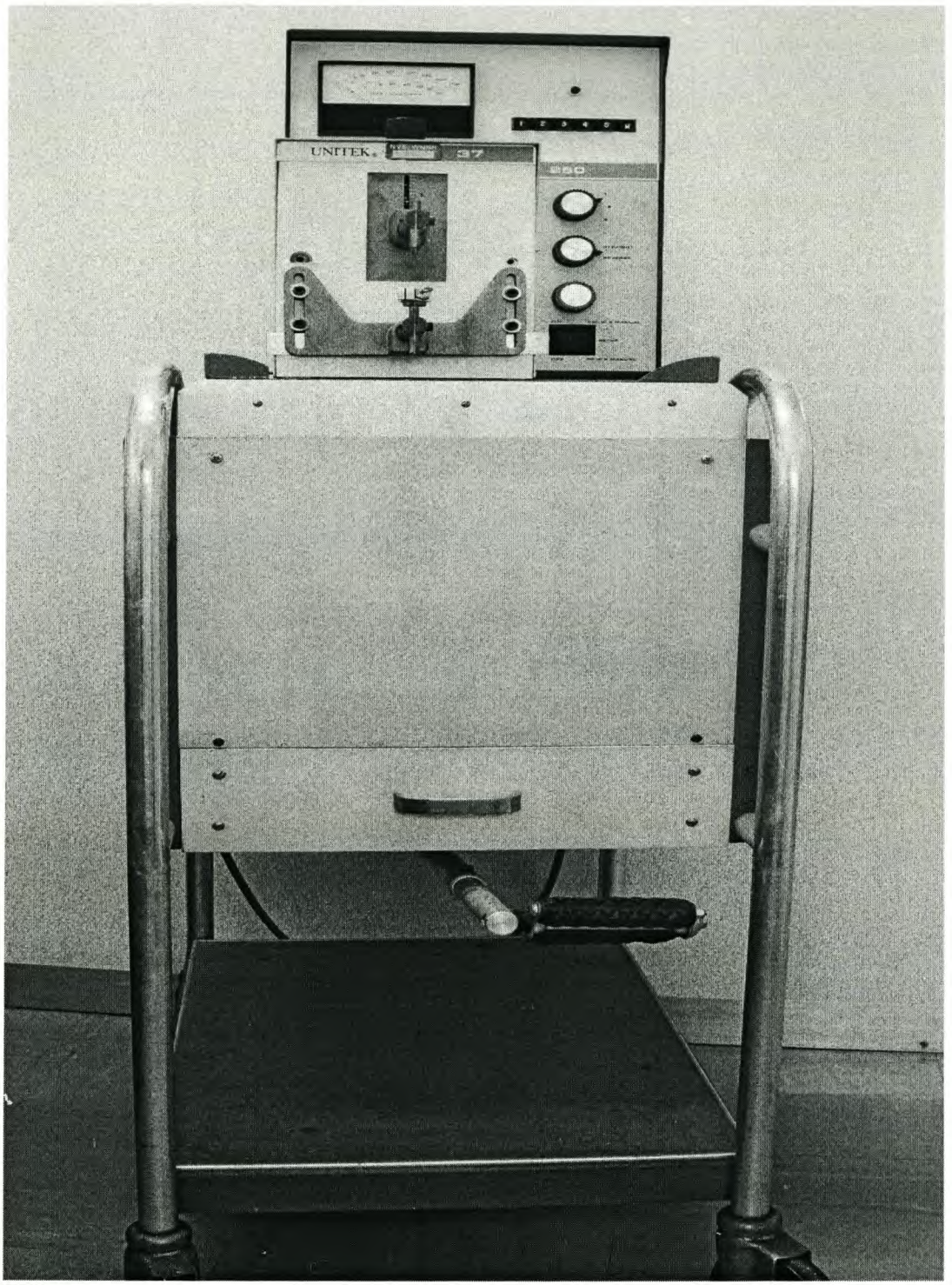
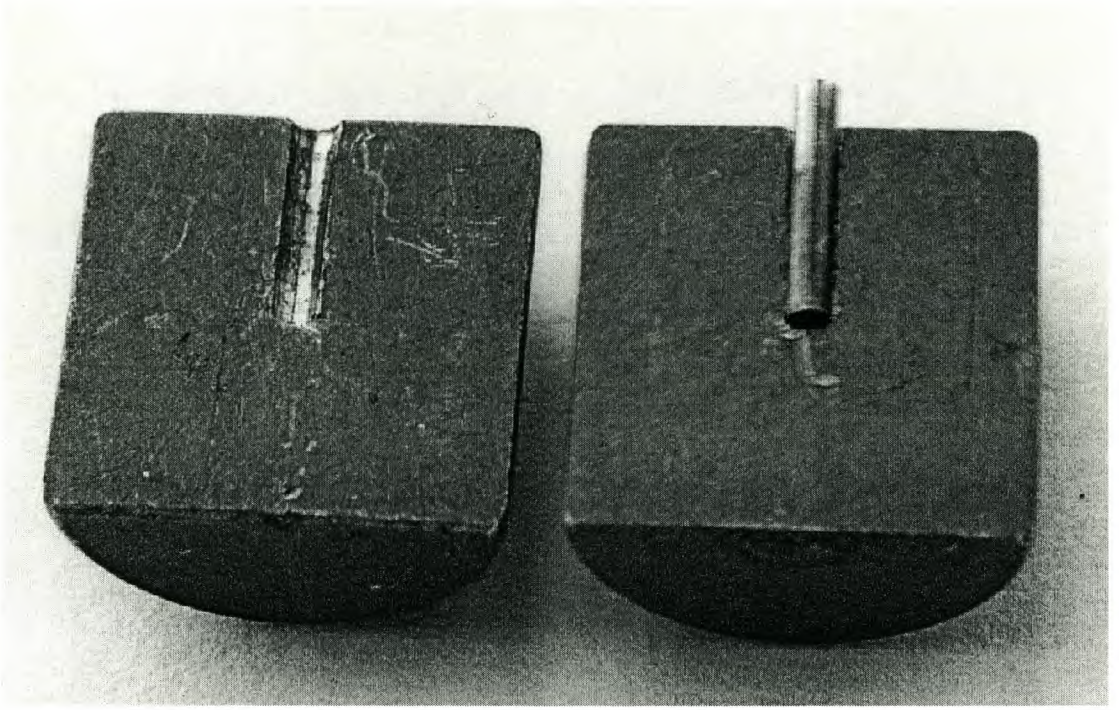
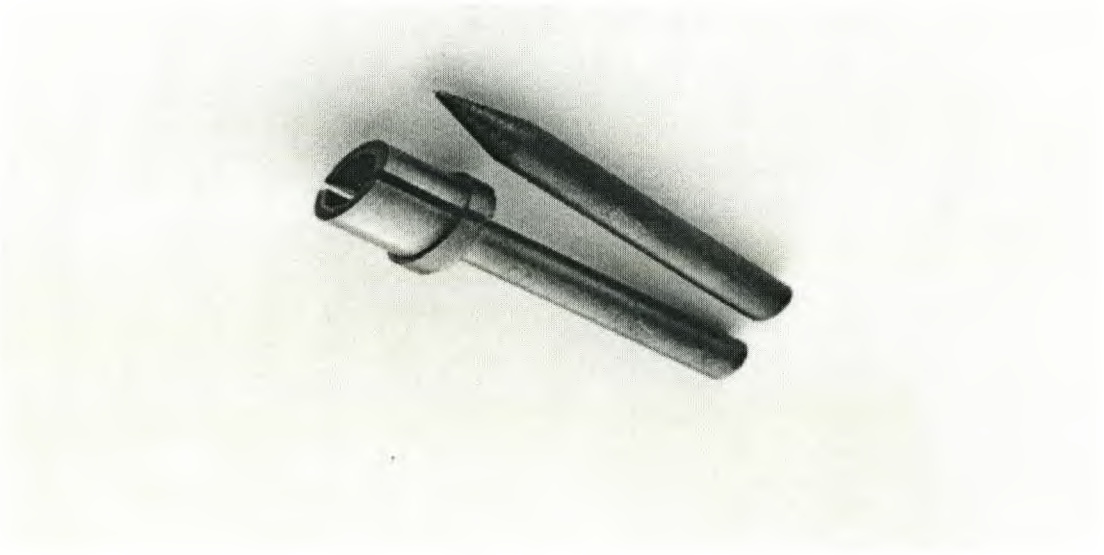


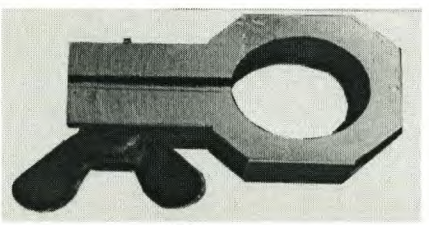
Fig. 5.3.5. The complete spot-welding machine.



(a)



(b)



(c)

Fig. 5.3.6 Components for the welding: (a) the two-piece tube holder; (b) the two electrodes; (c) the clamp.

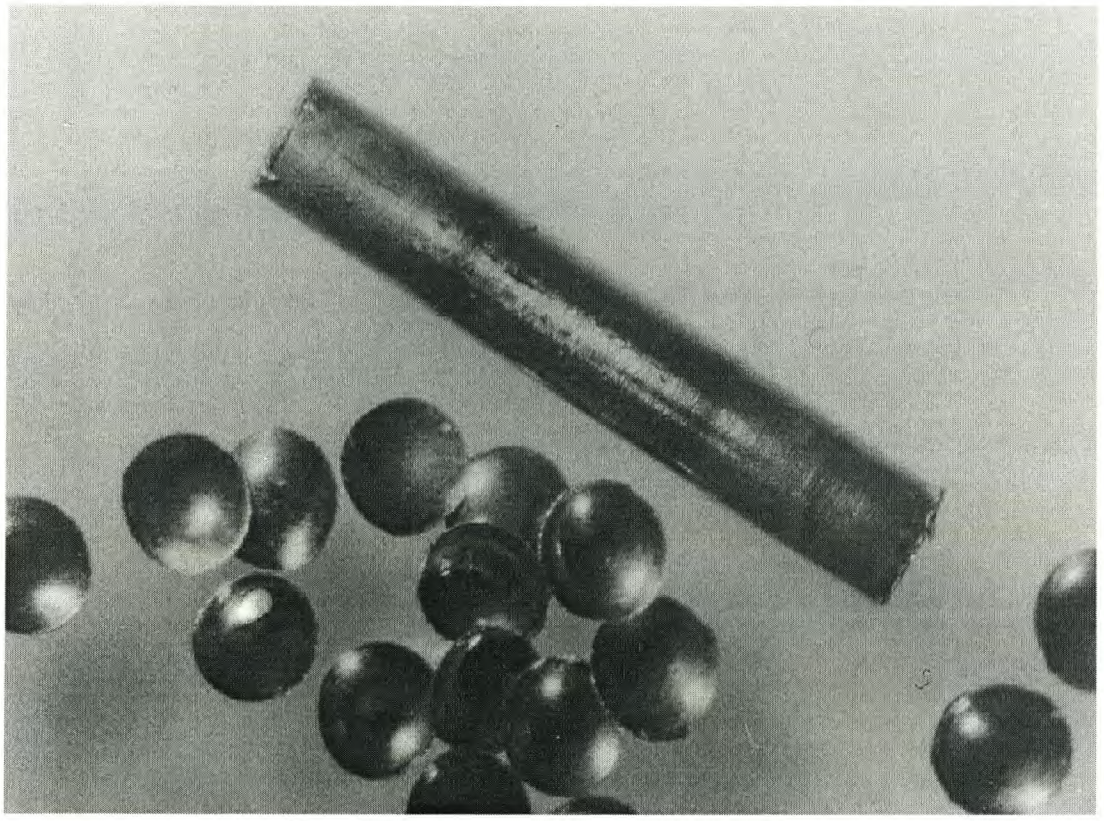


Fig. 5.3.7 Photomicrograph of the tube caps and a complete welded tube.

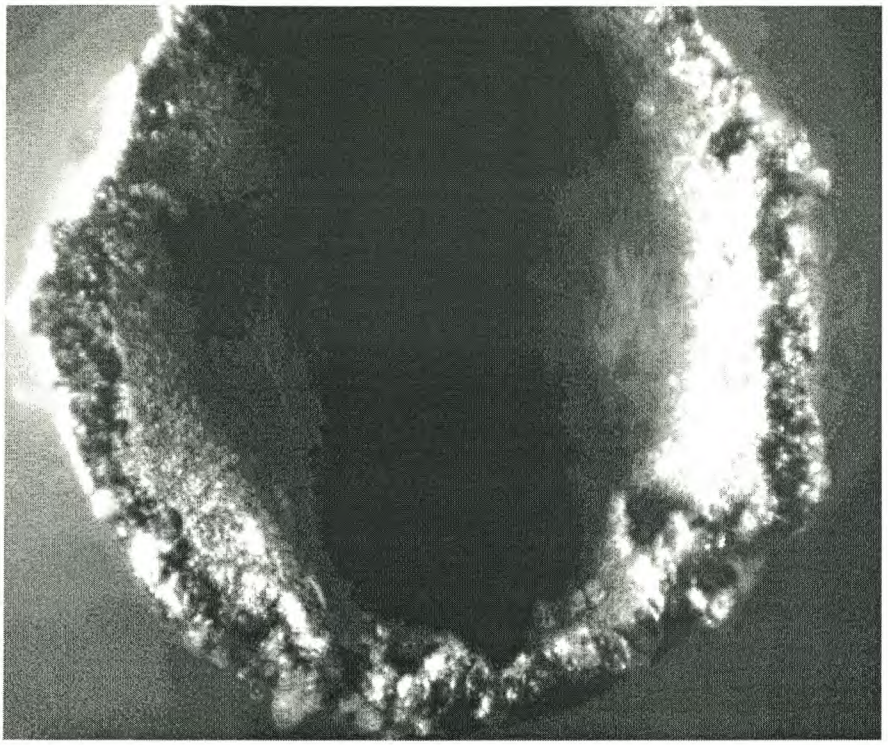


Fig. 5.3.8. Photomicrograph of the welding from top view.

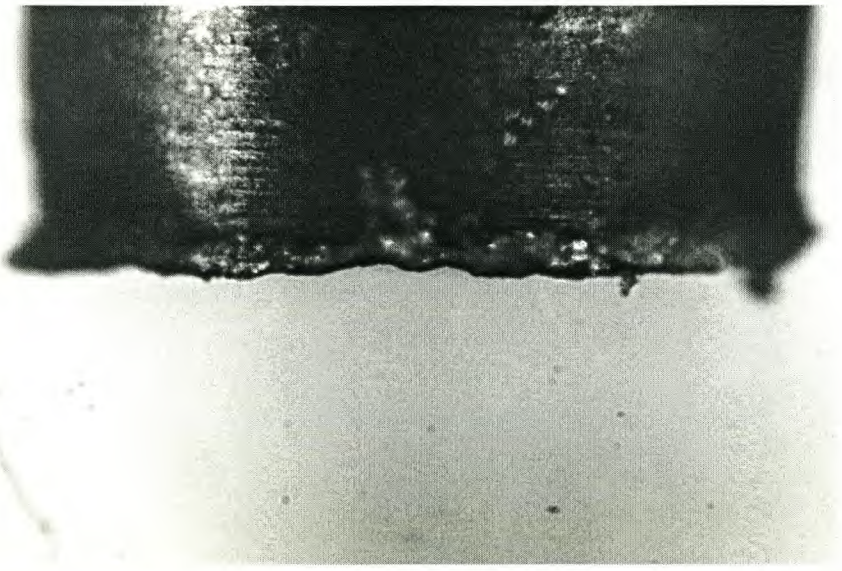


Fig. 5.3.9. Photomicrograph of the welding, side view.

5.4 CONCLUSIONS

5.4.1 Anion exchange resins for preparation of ^{103}Pd seeds

Although the results obtained from Amberlite IRA-93 resin are quite acceptable, to avoid any possible complications resulting from the resin conversion affecting a larger cross section of the beads than the inside diameter of the tube, a narrower size distribution range of beads can be used (550-600 μ, for example). Bio-Rad offers Bio-Rex MSZ resins which have high mechanical strength. For example, Bio-Rad MSZ1 resin is similar to AG 1 resin, but offers exceptional size uniformity. At least 99% of these resin beads are 550 microns ± 50 microns (30-40 mesh). In addition this resin is also available in Cl^- form, thus, there is no need for the conversion process, the drying and screening of the beads. The distribution coefficients for Pd on AG 1, are ca. ~1000 and >1000 in 1 M and 0.1 M HCl, respectively [25]. These values are very close to those obtained experimentally on the weakly basic anion exchanger resin Amberlite IRA-93 (Section 4.3.3).

The advantages of using the spherical resin than graphite plates are of a technical nature. Firstly, the sorption of ^{103}Pd on an ion exchanger is much easier than electroplating of ^{103}Pd, followed by cutting of the graphite sheet into small pieces with high precision and secondly, resin beads can be transferred much easier into the Ti tubes.

5.4.2 Spot- welding machine for enclosing the Ti tubes

Despite the facts that the Ti tubes were machined from Ti rods and that the caps punched by hand – resulting in some unevenness, the welding process seems extremely promising. The difficult part of the welding is placing the cap on the tube and good care has to be taken during this stage. Although the welding seems somewhat tedious for a mass production, it can easily satisfy local demand, is very economical with low maintenance cost operation.

CHAPTER 6

GENERAL SIGNIFICANCE OF THE RESEARCH RESULTS

6.1 The significance of the study

6.1.1 Analytical chemistry efficiency

The simplicity of the radiochemical separation of ^{103}Pd from a silver target, more than 90% yield, is a very important aspect of this study. This simplicity, in turn, resulted in the design of a simple radiochemical processing system easily operated by technicians. All the solutions are transferred to the hot cell using a single peristaltic pump. The valves used in this system are cheap and if they are damaged by radiation, they can be replaced easily with low cost.

Chemical quality control for final production is, essentially, unnecessary. Bombarding the silver target, several isotopes of Ag as well as Rh isotopes are produced which can be measured by a γ-spectrometry indicating the presence of natural silver in the final solution. Furthermore, should there be trace amounts of Ag in the final solution, it will be eluted when ^{103}Pd is sorbed on the Amberlite IRA-93 anion exchange resin from a 0.5 M HCl solution. For the same reason, there is no need for chemical quality control of Cu in the rhodium target separation.

Because of the simple electrolyte chosen for the Rh target preparation by electroplating, any additional and complicating chemical methods for recovering the Rh from the electrolyte bath, which may result in the loss of Rh and the preparation of a fresh bath, are avoided. Although anhydrous $Rh(ClO_4)_3$ is not available commercially, it can simply be prepared from soluble Rh salts that can either be recovered from the radiochemical waste or directly purchased.

Expensive power supplies for pulse or periodic reverse techniques are not required for electroplating purposes. The electroplating was performed using a standard DC power supply.

Rather than dissolving of Rh by alternating current, which is time consuming, the radiochemical separation of carrier-free ^{103}Pd from Rh and Cu is simple. Using a 5 cm × 1 cm column, the volume of reagents are very small and affords a small volume of radioactive waste. The solution obtained from the electrodissolution is directly used for the separation without any further dilution, evaporation or drying.

Although the radiochemical separation was designed for the separation of ^{103}Pd from Rh and Cu, it was also used for separation of Pd and Rh from Tc and Ru. The results from this separation procedure showed (manuscript submitted for publication) clearly that not only can Rh and Pd be separated from each other, but also from elements such as Tc, Ru, Nb, Y, Zr and Mo.

Compared to the commercial production of ^{103}Pd seeds using graphite pellets on which ^{103}Pd is plated and a laser or electron beam machine for welding the necessary Ti tubes, the methods presented in this study are much simpler, cheaper and more easily to carry out. For example, sorption of ^{103}Pd on spherical resin beads using column chromatography, followed by transferring the beads into the tubes by a designed funnel, is much easier than the electroplating of Pd on graphite followed by the cutting of the graphite sheet into small pieces that can fit into the Ti tubes. The only difficult part of the seed preparation, is to fit the end caps on to the Ti tubes. Using the methods presented here, this part of the production can be carried out by a technologist. Finally, the methods of this study for production of ^{103}Pd seeds to be used in brachytherapy are feasible, economical and should satisfy the local demand.

6.1.2 Financial implication

With regard to financial benefits, this project results are important for two reasons. Firstly, because of the local low cost of production of ^{103}Pd seeds, according to the newly developed methods, and secondly, as a result of the potential income from the purified ^{103}Pd or ^{103}Pd seeds. The present world wide demand for ^{103}Pd is very high and iThemba LABS plans to produce 2 Ci per week; the estimated revenue that can be generated by ^{103}Pd alone is R 3 million per annum and, in seed form, the income could increase tenfold.

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Publications and presentation

Part of this study has been submitted for publication to the Journal of RADIOANALYTICAL AND NUCLEAR CHEMISTRY. The titles are as follows:

1- *Separation of Pd-103 from Rh and Ag by macroporous AG MP-1 anion exchange resin from Ag targets.*

2- *Separation of Rh and Pd radioisotopes from other radioisotopes produced in interaction of Rh with C-12 and O-16 at 400 MeV.*

The whole study, entitled "The production of Pd-103 by proton-induced nuclear reaction on Ag and Rh. The preparation of Pd-103 seeds for brachytherapy of prostate cancer", was presented at iThemba LABS on 18 July 2002.

Journal of RADIOANALYTICAL AND NUCLEAR CHEMISTRY International Journal Dealing with all Aspects and Applications of Nuclear Chemistry

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March 25, 2002

Dear Dr. Aardaneh,

Your manuscript entitled:
Separation of Pd-103 from Rh and Ag by macroporous AG MP-1 anion exchange resin from Ag targets /reg.no. 5697/

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You are asked herewith to send us a letter stating whether your paper's content - not the paper itself - has been published entirely or in part or is under consideration by another journal.

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June 10, 2002

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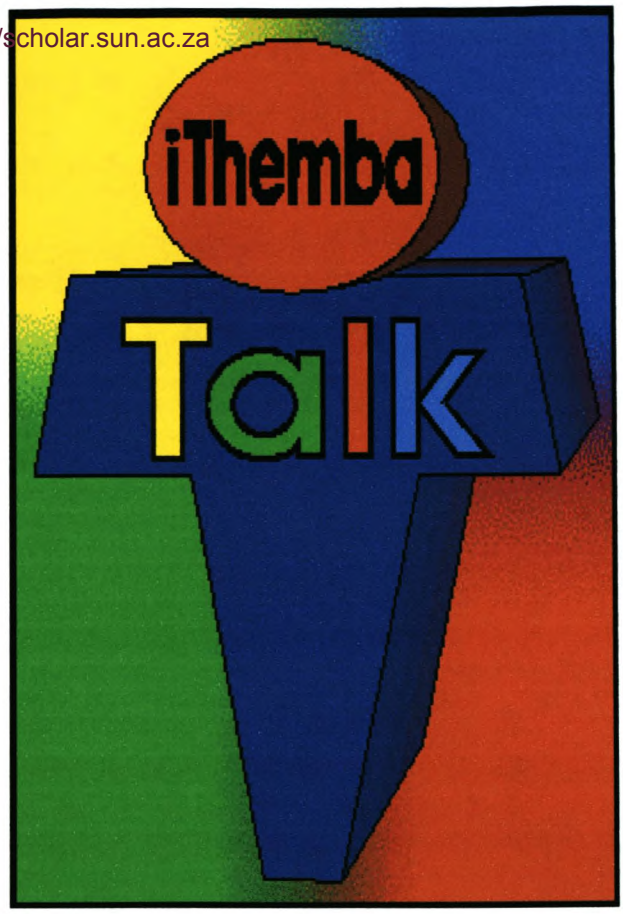

DATE: Thursday 18 July 2002

VENUE: Auditorium

TIME: 14:00

The first speaker at this session of iThembaTalk will be Khosro Aardaneh: "The production of Palladium-103 by proton induced nuclear reactions on Ag and Rh. The preparation of Palladium-103 seeds for brachytherapy of prostate cancer".

This will be followed by Lowry Conradie: "Motivation for a new ECR Ion Source for iThemba LABS".

Lastly Johann van Rooyen will talk about environmental radio-activity.