Terugbetaling van Radioisotopen in België

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VOORWOORD

Radioisotopen of beter radioactieve isotopen spreken tot de verbeelding. Voor de meesten zal het woord doen denken aan de lessen scheikunde en fysica of meer nog aan kerncentrales en nucleaire oorlogsvoering.

De afgelopen halve eeuw deden ook in de geneeskunde een aantal van die radio-actieve producten hun intrede. Nu zijn ze niet meer weg te denken in de diagnostische oppuntstelling van bijvoorbeeld schilklieraandoeningen of bepaalde kankers en in de behandeling met radiotherapie van diverse kankers. Jaarlijks gebeuren er zo in België ongeveer 570 000 diagnostische testen en een kleine 10 000 behandelingen met radioisotopen.

Veilig werken met radioisotopen (die qua straling erg kunnen verschillen) stelt omwille van de radio-activiteit ook bijzondere eisen aan het vervoer en de bewaring. In ons land waakt het Federaal Agentschap voor Nucleaire Controle (FANC) over de ganse veiligheidsketen van de radioactieve isotopen. Hierbij wensen we dan ook het FANC te danken voor de samenwerking en het ter beschikking stellen van de lijsten met nucleaire transporten van de medische radioisotopen. Dat leverde het KCE een hele papierberg op die met de RIZIV facturatiegegevens werden vergeleken om de Belgische praktijk te kunnen beschrijven.

Het doel van dit onderzoek was vooral de financiering van radioactieve isotopen in de geneeskunde kritisch door te lichten, en dit vanuit het standpunt van de verplichte ziekteverzekering. Het analyseren van het oordeelkundig 'evidence-based' diagnostisch en therapeutisch gebruik van radioistopen maakte geen deel uit van dit onderzoek.

De manier waarop therapeutisch gebruikte radio-isotopen in ons land door de verplichte ziekteverzekering vergoed worden is uniek. De producent stuurt de factuur naar het ziekenhuis en die stuurt ze verder naar het ziekenfonds dat dan betaalt. Het onderzoek heeft zich toegespitst op die onderzoeken met een zichtbare stijging in de uitgaven voor de ziekteverzekering over de laatste jaren. Daarnaast werd onderzocht wat hetzelfde, soms zelfs Belgisch product, kost in ons omringende landen en hoe dat daar de financiering van radioisotopen geregeld is.

We wensen de fabrikanten, de distributeurs en de transporteurs van radioisotopen, de ziekenhuisadministraties en het FANC warm te danken voor hun medewerking.

Jean-Pierre Closon
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Samenvatting

INTRODUCTIE

Radioactieve isotopen voor gebruik in de geneeskunde worden aangemaakt in een kernreactor of een cyclotron. Sommige isotopen kunnen worden gebruikt in het laboratorium, voor klinische diagnostiek of voor de behandeling van tumoren.

Het doel van dit onderzoek was vooral de financiering in België van radioactieve isotopen in de geneeskunde kritisch te evalueren, en dit vanuit het standpunt van de verplichte ziekteverzekering. De laboratoriumtesten met radioisotopen werden niet bestudeerd in dit project. Radioisotopen voor therapeutisch gebruik zorgen wereldwijd slechts voor een tiende van de totale productie van radioisotopen gebruikt voor medische doeleinden, terwijl hun marktwaarde ongeveer een vijfde bedraagt van de totale marktwaarde van verhandelde radioisotopen. Ons onderzoek heeft zich toegespitst op de radioisotopen waarvoor de uitgaven voor de ziekteverzekering de laatste jaren zichtbaar is toegenomen.

De straling en de halfwaardetijd van radioisotopen stellen bijzondere eisen aan het vervoer en de bewaring van de isotopen. In ons land heeft het Federaal Agentschap voor Nucleaire Controle (FANC) de opdracht te waken over de veiligheidsketen van de radioactieve isotopen.

METHODOLOGIE

Voor deze studie werden door het KCE een aantal gegevensbronnen voor het jaar 2005 met elkaar gekoppeld. Volgende instanties werden gecontacteerd voor het verkrijgen van relevante gegevens:

- het RIZIV voor de jaarlijkse uitgaven per nomenclatuurcode voor diagnostische en therapeutische radioisotopen, voor de verstrekkingen van urologen, radiotherapeuten en nuclearisten, en voor de pseudo-codes gebruikt voor radioisotopen per kwartaal en per instelling.
- het FANC voor de listing op maandelijkse basis van de vervoerde radioactieve producten in België met datum, afzender en bestemmeling, isotoop en radioactiviteit.
- de producent (IBt, Seneffe) en verdelers (Mallinckrodt/Tyco Healthcare/Covidien, Oncura UK/Amersham Health/GE Healthcare, Bristol-Myers Squibb Belgium, Nordion, Canberra, Nucletron/Bogman Medical Equipment, Varian Medical Systems) voor de lijst van hun Belgische klanten en de verkochte producten.
- talrijke ziekenhuizen voor de aankoopfacturen voor ^{125}Jodium (^{125}I) zaden en ^{192}Iridium (^{192}Ir).
- de Belgische vereniging voor Nucleaire Geneeskunde, en de Belgische Beroepsvereniging der Specialisten in Kerngeneeskunde binnen het Verbond der Belgische Beroepsverenigingen van Geneesheren-Specialisten voor een gedetailleerde bevraging naar de specifieke testen uitgevoerd per radioisotoop. Participatie aan de bevraging was volgens deze verenigingen niet haalbaar en deze bevraging werd bijgevolg niet uitgevoerd.

De combinatie van onzorgvuldig coderen bij de facturatie en het grote aantal bestaande pseudo-codes, waarvan het merendeel niet meer actueel is, bemoeilijkte het koppelingsproces. Bovendien bleken de vervoersdocumenten van één transporteur voor ^{125}I zaden voor een periode van meerdere maanden niet aangegeven bij het FANC. Dit kon worden opgelost in samenwerking met het FANC. Aan de hand van de vrachtbrieven konden wel niet alle leveringen aan ziekenhuizen in detail geanalyseerd en gekoppeld worden. Het is namelijk zo dat slechts voor bepaalde grotere leveringen de vrachtbrief in detail de isotopen en hun radioactiviteit dient weer te geven.

UITGAVEN VOOR RADIOISOTOPEN IN BELGIE

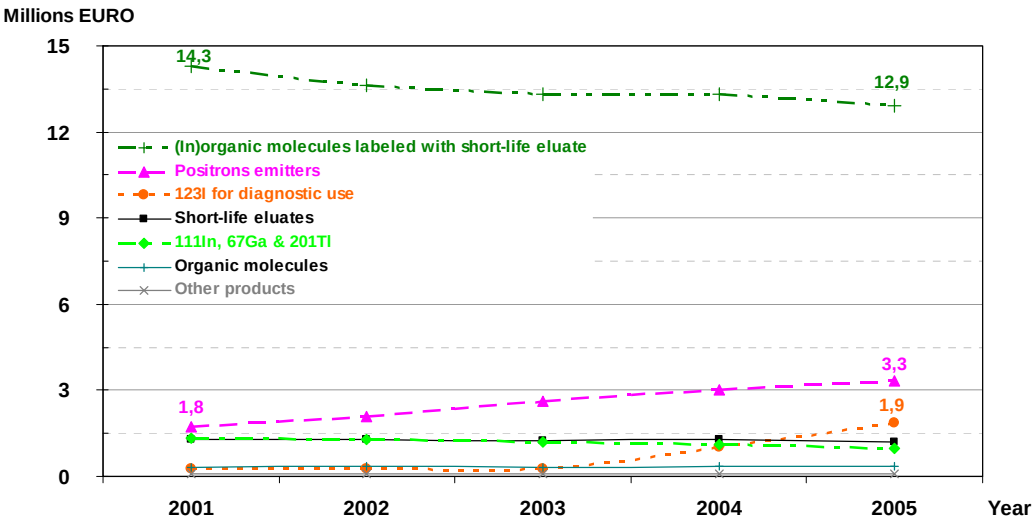
In ons land is de vergoeding van isotopen vervat in het hoofdstuk VI van de terugbetaalde geneesmiddelen. Onder hoofdstuk VI alinea 2 worden de radioisotopen voor therapeutische doeleinden opgelijst onder terugbetalingsgroep A-37. Onder hoofdstuk VI alinea 3 worden de radioisotopen voor diagnostische doeleinden opgesomd onder terugbetalingsgroep B-205. Er bestaat een duidelijk verschil in de manier waarop diagnostische versus therapeutische radioisotopen worden vergoed door de verplichte ziekteverzekering. Voor diagnostische radioisotopen wordt de tegemoetkoming forfaitair bepaald in categorie B per radioisotoop, groep van isotopen, of per manier van koppeling van het radioisotoop (zie bijlage 2 van het wetenschappelijk rapport). Radioisotopen volgen een procedure voor terugbetaling onder de RIZIV Commissie Tegemoetkoming Geneesmiddelen via een "Technische Raad voor Radioisotopen" opgericht onder de wet van 27 december 2005. De samenstelling van deze "Technische Raad voor Radioisotopen" werd pas via KB van 28 december 2006 vastgesteld. De leden van die raad werden nog niet benoemd, waardoor de juridische onzekerheid blijft.

Het gefactureerde bedrag voor een individueel gebruik wordt volledig door de verzekering vergoed. Alleen voor ^{125}Jodium en ^{103}Palladium bestaan beperkingen wat betreft indicatie. Voor oplossing van ^{90}Yttrium chloride is bovendien een goedkeuring door de verzekeringsinstelling nodig. De producent of de verdeler is dus vrij de prijs van de goederen te bepalen en stuurt de factuur naar het ziekenhuis, dat dezelfde factuur dan verder stuurt naar de verzekeringsinstelling zonder controlestap. Voor een bron gebruikt voor meerdere patiënten, wordt de factuur soms verdeeld over de behandelde patiënten.

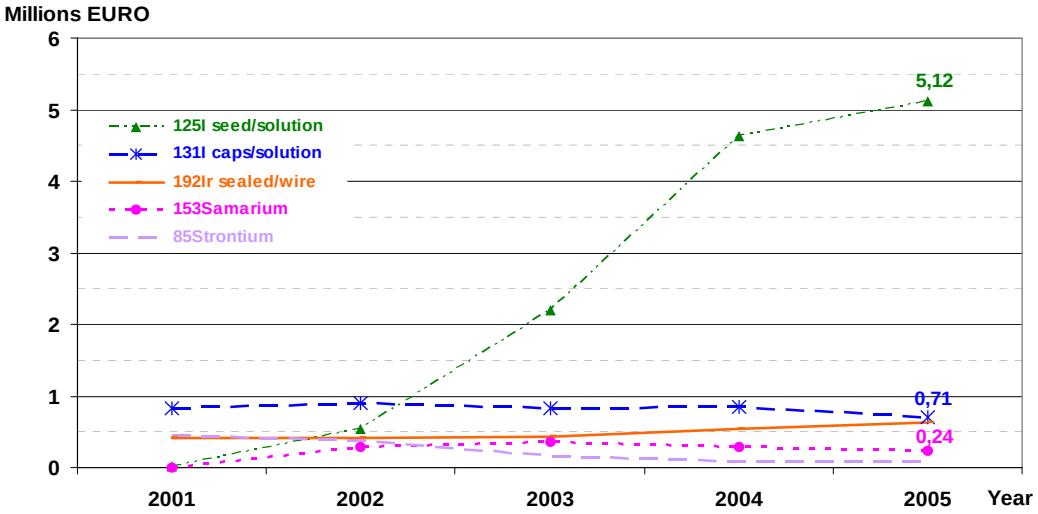
De totale RIZIV uitgaven voor radioisotopen bedroegen €27,5 miljoen in 2005. Voor diagnostisch gebruik (Figuur A) stegen de uitgaven beperkt van €19,4 miljoen in 2001 naar €20,7 miljoen in 2005. De uitgaven voor therapeutisch gebruik van radioisotopen (Figuur B) stegen daarentegen met 300% sinds 2001, van €1,7 miljoen naar €6,8 miljoen.

Testen gebaseerd op het ^{99m}Technetium zorgen voor het grootste volume en blijven de belangrijkste uitgavenpost binnen de diagnostische isotopen, ook al bestaat er een licht dalende trend in volume en uitgaven. Op de tweede plaats, en met continu stijgende uitgaven, komt het ^{18}Fluoro-deoxyglucose (^{18}FDG) dat voor Positron-Emission Tomography (PET) gebruikt wordt. Opvallend is ook de recente stijging in de uitgaven voor de ^{123}I-DATscan®, gebruikt in geval van diagnostische twijfel bij de ziekte van Parkinson. Het betreft hier een dure test die vooral in een twaalftal ziekenhuizen gebeurt.

Figuur A. RIZIV uitgaven voor diagnostische radioisotopen



Figuur B. RIZIV uitgaven voor therapeutische radioisotopen



De belangrijkste stijging in de uitgaven voor radioisotopen werd gezien voor het therapeutisch gebruik van ^{125}I zaden voor brachytherapie, bijna uitsluitend gebruikt door urologen bij beperkte vormen van prostaatkanker. Voor 2005 werden ^{125}I zaden terugbetaald voor 765 behandelingen van prostaatkanker. Voor gemiddeld een 80-tal ^{125}I zaden per behandeling voor prostaatkanker varieerde de prijs tussen €4150 en €8014 met een mediaan van €6890. De prijs van dezelfde zaden, geproduceerd in ons land, bedraagt in Frankrijk en Nederland respectievelijk €3530 en €3600, alle taksen inbegrepen.

Talrijke ziekenhuizen springen slordig om met de codering van de facturen voor ^{125}I zaden, zonder dat dit een rechtstreeks financieel gevolg heeft. Indien men zich uitsluitend baseert op de pseudo-code voor ^{125}I zaden, verkrijgt men bijgevolg een vertekend beeld van het aantal gevallen behandelde prostaatkanker. Het gebruik van de pseudo-codes voor facturatie van therapeutische radioisotopen zorgt voor problemen bij de meeste gebruikers: niet alleen bestaat er verwarring tussen de verschillende vormen van eenzelfde product maar ook tussen de verschillende producten. De isotoop pseudo-code en de meerdere verstrekkingscodes voor de ingreep die door de uroloog en radiotherapeut samen wordt uitgevoerd, worden bovendien ook niet samen gefactureerd.

Een distributeur paste de prijs per ^{125}I zaad aan volgens het aantal bestelde zaden om te komen tot een vast totaalbedrag per factuur van €6328,20. Twee andere distributeurs van ^{125}I zaden vermeldden op de facturen noch het aantal zaden, noch de radioactiviteit. Dit ging systematisch gepaard met een abnormaal hoog bedrag op de factuur. Dit bleek een compensatie te zijn voor het ter beschikking stellen van software voor optimalisatie van de bestraling met ^{125}I zaden, materiaal, en andere vormen van dienstverlening.

Een tweede radio-isotoop voor therapeutisch gebruik dat we nader onderzochten was ^{192}Iridium. We constateren een grote variabiliteit tussen de ziekenhuizen in de manier van aanrekening bij het RIZIV. Eenzelfde bron wordt namelijk gedurende drie tot vier maanden gebruikt voor zeer tijdelijke bestraling bij meerdere patiënten over meerdere sessies. Facturatie gebeurt soms voor de volledige kost ten laste van de eerst behandelde patiënt, soms verdeeld over alle of een vast aantal patiënten behandeld gedurende één trimester. Bijgevolg kan men op basis van de RIZIV gegevens geen duidelijk beeld krijgen van het aantal behandelde patiënten, het aantal behandelingen en de gemiddelde terugbetaling per behandelingssessie.

^{153}Samarium-Lexidronam (Quadramet®) wordt steeds aan €1303,32 per patiënt gefactureerd door de firma Schering onafhankelijk van de bestelde dosis.

INTERNATIONALE VERGELIJKING

Literatuurgegevens over de consumptie of het gebruik van radioistopen in andere landen werden slechts gevonden voor het Verenigd Koninkrijk en voor Nederland. Daaruit bleek dat vooral het volume van diagnostische beeldvormingsprocedures sterk is toegenomen in de laatste 10 tot 20 jaar. Het aantal therapeutische procedures bleef daar vrij stabiel. Beeldvorming van het beendergestel, de longen en het cardiovasculair systeem waren het meest frequent. De meest frequente therapeutische procedure in beide landen was de behandeling van hyperthyroidie met ^{131}I. Van brachytherapie met ^{125}I is er in beide studies (nog) geen sprake.

De vier landen die werden opgenomen in het overzicht van financieringssystemen voor radioisotopen (Nederland, Frankrijk, Italië, UK) evolueren allen naar een *per case* financiering.

In Nederland wordt de terugbetaling van diagnostische en therapeutische radioisotopen geregeld via de tarieven voor de Diagnose Behandel Combinaties (DBCs). Deze omvatten een component voor de dekking van ziekenhuiskosten en een honorarium voor de arts. Radioisotopen worden verondersteld gedekt te worden door de ziekenhuiskostencomponent van de DBC. De prijs van ^{125}I in Nederland is ongeveer €45,05/zaad, wat overeenkomt met een totaalkost van €3 604 voor 80 zaden ^{125}I (gemiddeld verbruik).

In Frankrijk zit de terugbetaling van radioisotopen meestal ook vervat in het *per case* tarief. Sommige zeer dure isotopen staan op de lijst voor dure geneesmiddelen en worden gefinancierd bovenop het *per case* tarief. Voor deze isotopen gelden maximumtarieven. Voor brachytherapie van de prostaat is het bedrag voor ^{125}I geplafonneerd op 3 970.80€, wat overeenkomt met een behandeling met maximaal 90 zaden van €44,12 per zaad.

Italië heeft een sterk gedecentraliseerd financieringssysteem voor gezondheidszorg. De regio's bepalen autonoom de tarieven in het *per case* financieringssysteem. Radioisotopen worden over het algemeen vergoed als onderdeel van de tarieven per aandoening, al zijn er uitzonderingen in sommige regio's.

In het VK worden diagnostische radioisotopen vergoed via de *per case* vergoeding. Radiotherapie wordt wellicht pas opgenomen in het *per case* financieringssysteem in 2009. Er is momenteel discussie in de VK of het wenselijk is de isotopen binnen het *per case* tarief te vergoeden.

CONCLUSIES

Het huidige systeem van pseudo-codes voor radioisotopen voor diagnostische doeleinden is niet transparant en laat geen analyse toe van het gebruik van een specifiek isotoop of gekoppeld isotoop voor een bepaalde test.

De vrachtbrieven voor de leveringen aan ziekenhuizen bevatten niet steeds in detail de inhoud aan therapeutische radioisotopen.

De totale RIZIV uitgaven voor radioisotopen bedroegen €27,5 miljoen in 2005. Voor diagnostisch gebruik was de uitgavenstijging beperkt. De uitgaven voor therapeutisch gebruik van radioisotopen stegen daarentegen met 300% sinds 2001, tot €6,8 miljoen in 2005.

Deze stijging is bijna uitsluitend te wijten aan een toename in het gebruik van brachytherapie voor de behandeling van lokale vormen van prostaatkanker. Deze vorm van behandeling gebeurt in talrijke centra, met soms een zeer laag volume.

Tachtig ^{125}I zaden die daarbij gebruikt worden kosten in België vaak exact €6900 terwijl dezelfde zaden, geproduceerd in België, in Frankrijk en Nederland ongeveer €3600 kosten.

Dure software, materiaal, en andere diensten werden in 2005 aangerekend via hogere factuurbedragen voor therapeutische radioisotopen.

BELEIDSAANBEVELINGEN

- Een terugbetaling op factuur van therapeutische radioisotopen zonder controle staat in contrast met een doelmatig gebruik van middelen in de gezondheidszorg.
- Volgende alternatieve opties voor de vergoeding van therapeutische isotopen zijn mogelijk:
    - Een all-in forfaitair bedrag voor zowel honoraria, isotoopkost, software en materiaal alsook eventuele noodzakelijke bijkomende diensten.
    - Een terugbetaling op factuur, maar met een meer verantwoorde en door het RIZIV bepaalde tegemoetkoming in lijn met de internationaal geldende prijzen. Voor gemiddeld 80 ^{125}Iodium zaden voor prostaat brachytherapie kan de prijs bijvoorbeeld dalen van ongeveer €6900 naar €3600, een prijs die in Nederland en Frankrijk gehanteerd wordt.
- Alle aanrekeningen dienen voldoende detail te geven naar de geleverde hoeveelheid (eenheidsprijs en aantal) en de radioactiviteit.
- Ziekenhuizen dienen zorgvuldiger om te springen met het gebruik van de nomenclatuur voor de aanrekening van therapeutische radioisotopen. Zo kan met komen tot meer betrouwbare gegevens voor de gemiddelde RIZIV uitgaven per behandeling, patiënt of sessie.
- Een wettelijk verplichte vermelding van alle therapeutische isotopen en hun radioactiviteit bij elke ziekenhuislevering, ingebracht in de FANC database, en electronisch overgemaakt om te koppelen met de facturatiegegevens van isotopen aan het RIZIV, zou voor het RIZIV een belangrijk hulpmiddel zijn om de in dit project gedetecteerde problemen te vermijden.
- Bij de herziening van de financieringsmechanismen voor therapeutische radioisotopen dient de huidige lijst van therapeutische pseudo-codes geactualiseerd te worden.
- Ter beraadslaging over en uitvoering van dit rapport en haar beleidsaanbevelingen is het wetenswaardig dat, in uitvoering van de wet van 14-07-1994, een "Technische raad voor radioisotopen" in december 2006 werd opgericht.

ONDERZOEKSAGENDA

Meer detailonderzoek is gewenst voor de 570 000 diagnostische testen die elk jaar met radioisotopen plaats vinden. Een meer gedetailleerde nomenclatuur zou een analyse van het gebruik van een specifiek isotoop of gekoppeld isotoop per orgaan of functie mogelijk maken.

Voor prostaatkanker met een beperkt volume bestaan er meerdere management opties: "watchful waiting", heelkunde, 3D-conformele externe radiotherapie, IMRT (intensity-modulated radiotherapy), brachytherapie e.a. Voor de ontwikkeling van een beleid dat efficiënte behandeling van kanker nastreeft, is het van belang deze opties te evalueren met een HTA. Het lijkt ons gepast dat een multidisciplinair oncologisch consult voorafgaat aan de behandelingskeuze van prostaatkanker.

De uitbreiding van brachytherapie naar behandeling van borstkanker vraagt ook een grondige evaluatie.

Scientific summary

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1 INTRODUCTION

1.1 INTRODUCTION TO RADIOISOTOPES

Radioisotopes in medicine (or radiopharmaceuticals) can be used both for diagnostic and therapeutic purposes. In developed countries each year about 2% of the population have a diagnostic exam using such technique. The frequency of therapy with radioisotopes is about one tenth of this. The use of radioisotopes in diagnosis is growing at over 10% per year.(http://www.world-nuclear.org/info/inf55.html). Radioimunoassay (RIA) is a very sensitive and specific in vitro lab method. In developed countries, RIA has largely been replaced by non-radioactive immunoassays.

A radioactive isotope or radioisotope is an unstable atom with a combination of neutrons and protons, most often produced artificially. Radioisotopes can be manufactured by neutron activation in a nuclear reactor. This involves the capture of a neutron by the nucleus of an atom resulting in an excess of neutrons (neutron rich). Some radioisotopes are manufactured in a cyclotron in which protons are introduced to the nucleus resulting in a deficiency of neutrons (proton rich).

The nucleus of a radioisotope usually becomes stable by emitting an alpha particle or positron. These particles may be accompanied by the emission of energy in the form of electromagnetic radiation known as gamma rays. This process is known as radioactive decay.

Nuclear medicine was developed in the 1950s by physicians with an endocrine emphasis, initially using iodine-131 to diagnose and then treat thyroid disease. In recent years specialists have also come from radiology, as dual PET-CT procedures have become established.

1.2 DIAGNOSTIC TECHNIQUES

Radioactive tracers which emit gamma rays from within the body are generally short-lived isotopes linked to chemical compounds which permit specific physiological processes to be scrutinised. Targets for radiolabeled probes can be receptors, enzymes, transporters or antigens. They can be given by injection, inhalation or orally. The mean effective dose is 4.6 mSv per diagnostic procedure. Diagnostic radioisotopes and their characteristics are listed in Appendix 1.

Organ malfunction can be indicated if the isotope is either partially taken up in the organ (cold spot), or taken up in excess (hot spot). If a series of images is taken over a period of time, an unusual pattern or rate of isotope movement may indicate malfunction in the organ. The radioactive tracers can be located in the body using a gamma camera or a PET camera.

1.2.1 Gamma camera based detection

The planar gamma camera detects single photons and builds up an image from the points from which radiation is emitted. The photons emitted by the patient may be acquired as static images (eg bone, liver, thyroid scan) or dynamic images. Sequential images are collected when the distribution of the radionuclide in the organ is changing rapidly and it is important to pick up this change, eg vascular flow of the radionuclide through an organ like the brain or the kidney. Gated images represent a special case of dynamic images of a moving organ like the heart where the sequence of images is synchronized from the start of every new cardiac cycle and triggered by the R-peak of the ECG. Data are thus divided into a fixed number of frames so that the wall motion can be decomposed and a left ventricular ejection fraction can be repetitively calculated.

A further development is single photon emission computer tomography (SPECT). To acquire SPECT images, a single, two or three gamma cameras are rotated around the patient. The data are then processed by a computer to give cross-sectional views of the organ, eg the brain or the heart.

Cardiac gated acquisitions (triggered by ECG) are possible with SPECT, just as with planar imaging techniques such as multigated acquisition (MUGA).

The most frequently used isotope for gamma camera based detection is ^{99m}Technetium, accounting for at least 90% of all procedures. It has favourable characteristics for a nuclear medicine scan: a half-life of 6 hours, emission of accurately detectable 140 keV gamma rays and no high energy beta emission, it can be incorporated into a range of molecules thus concentrating it in the tissue or organ of interest. Furthermore, it can be generated from ^{99}Molybdenum which decays to ^{99m}Tc and has a half-life of 66 hours. Such a generator can be supplied once a week to hospitals from the nuclear reactor. ^{99m}Tc is then washed out when needed ('on tap'). It is obvious that after 5 days less ^{99m}Tc is generated compared with day 1.

Commercial kits are available to link ^{99m}Tc to the appropriate chemical compound before use. ^{99m}Tc is most frequently used to image the skeleton (estimated at 75% of the test volume), eg linked to methylenediphosphonate (MDP), which has a high affinity for the bone mineral hydroxyappatite. Another large volume use is heart imaging, both assessments of the left-ventricular ejection fraction (LVEF) as well as the myocardial perfusion. ^{99m}Tc labeled red blood cells are typically used to measure the LVEF using MUGA. Heart muscle imaging can be performed using ^{99m}Tc eg coupled to isonitriles (sestamibi). Also ^{201}Thallium, taken up by viable myocardial cells, can be used for this purpose.

^{99m}Tc can be chelated in diethylenetriaminepentaacetic acid (DTPA) for kidney and brain scans. ^{99m}Tc sulfur colloid kits are used for the liver/spleen imaging. ^{99m}Tc aggregated albumin is used for lung scans. For thyroid imaging ^{99m}Tc pertechnetate is the main radiopharmaceutical while the use of ^{131}I is now mainly for therapy.

1.2.2 Positron Emission Tomography

A more recent development is Positron Emission Tomography (PET) which is a more precise and sophisticated technique using isotopes produced in a cyclotron. A positron-emitting radionuclide is introduced, usually by injection, and accumulates in the target tissue. As it decays it emits a positron, which promptly combines (annihilation) with a nearby electron resulting in the simultaneous emission of two 511keV gamma rays in nearly opposite directions. The high energy of the photons results in much less scatter and attenuation compared with conventional nuclear imaging. The gamma rays are detected by a series of detectors placed in a ring around the patient.

The main radiopharmaceutical used for PET imaging is Fluoro-deoxy glucose (FDG), containing ^{18}F. FDG is incorporated into cells without being broken down, and indicates cell metabolism. As ^{18}F is produced in a cyclotron and has a half-life of just under two hours, the procedure is to be undertaken within 2 hours of a cyclotron. FDG-PET has an added value in the diagnosis and staging of specific cancers with an accelerated glucose metabolism. Co-registration of images based on CT (PETCT) or MRI together with FDG-PET is increasingly being used to define tumor volumes for radiation treatment planning. Other uses are in brain and cardiac imaging, eg studies of myocardial viability.

1.3 THERAPEUTIC USE

The number of therapeutic procedure using radioisotopes is much lower compared with diagnostic procedures. The isotope used as radiation source for internal radiotherapy is usually a beta emitter. The route of administration of the radioisotope can differ.

^{131}Iodine targetting the thyroid is given intravenously. It is commonly used to treat thyroid cancer but can also be used to treat non-malignant thyroid disorders.

In brachytherapy (also known as 'curietherapy') implants are placed inside or very close to the tumor, interstitial as for local early stage prostate cancer, or intracavitary as in cervical cancer. Brachytherapy acts short-range, controlling local cellular growth.

Such internal radiotherapy differs from external radiotherapy, where the source of irradiation remains external to the body. Brachytherapy can be transient or permanent. In transient brachytherapy a temporary high dose rate can be administered a single or multiple times using an afterloading device. For permanent prostate brachytherapy close to 80 radioactive 'seeds' of the size of a grain of rice are placed in the prostate tissue using a needle and while the patient is under general or local anaesthesia. The exact position of each seed is visually controlled using an ultrasonic probe. The implanted seeds deliver a precise radiation dose to the prostate while sparing the surrounding healthy tissues.

The first seeds were made of ^{103}Palladium but today only ^{125}Iodine is still used. Sometimes external radiotherapy is combined with brachytherapy.

^{192}Iridium implants are used especially in the head and breast, but have also been used for prostate cancer. They are produced in wire form and are introduced through a catheter to the target area. After administering the correct dose, the implant wire is removed to shielded storage.

2 EXPENDITURES FOR RADIOISOTOPES IN BELGIUM

2.1 LEGAL FRAMEWORK

In Belgium, the protection of the population and the environment against ionizing radiation is coordinated by the AFCN/FANC (Agence Fédérale de Contrôle Nucléaire/ Federaal Agentschap voor Nucleaire Controle). This agency was created by article 2 of the law of 15 April 1994.

The Royal Decree of 20 July 2001 (and its later modifications) further defines the way the population, the employee's and the environment are protected against the dangers of ionizing radiation. The administration for medical purposes of radioisotopes is restricted to class II institutions. The Royal Decree defines the conditions for institutions to obtain a class II license, as well as the qualifications for specific types of experts. The import, production and sales of radioisotopes for "*in vivo*" or "*in vitro*" use require a licence from the AFCN/FANC. In case the radioisotope has a therapeutic use, it can only be marketed after registration in accordance with the Royal Decree of 3 July 1969 on the registration of medicines. The producers or importers of radioisotopes for medical use have to deliver the radioisotopes directly, without commission agent, to a licensed medical doctor or veterinarian, or the licensed pharmacists or clinical biologists in case of isotopes for "*in vitro*" use. Any transport of radioisotopes is to be communicated to the AFCN/FANC on a monthly basis with the date, addressee, nature and quantity of the transported radioisotopes. The AFCN/FANC can define requirements with regard to the hospitalisation of patients having been treated with radioisotopes. Also procedures for burying or burning bodies are given.

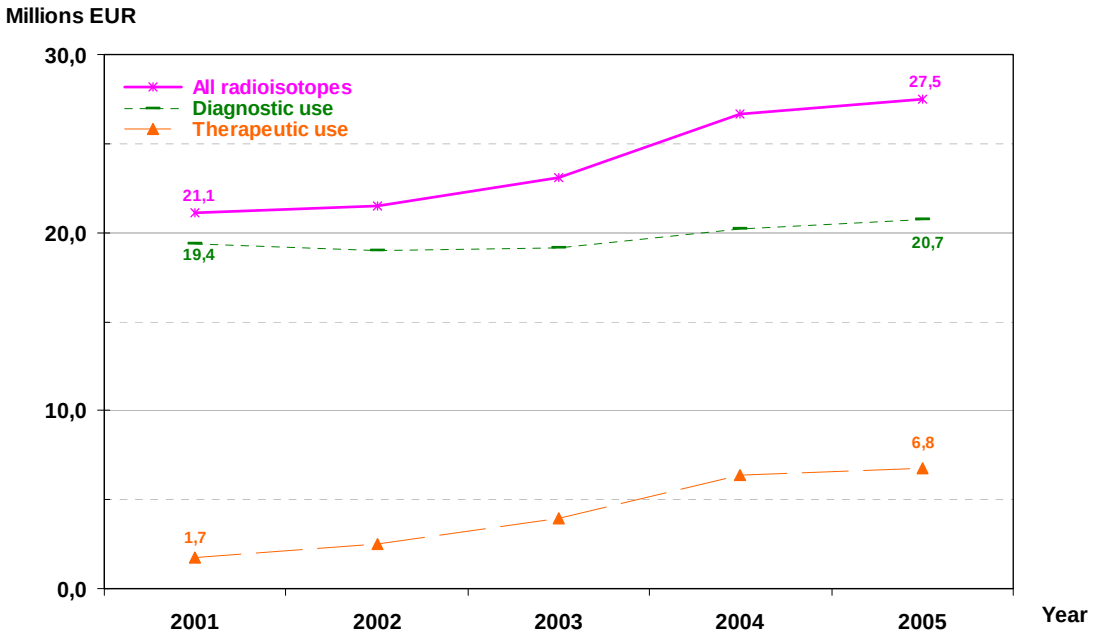
The reimbursement of isotopes in included under RIZIV/INAMI chapter VI on the reimbursement of medicines (www.riziv.fgov.be / www.inami.fgov.be). Under chapter VI alinea 2 radioisotopes for therapeutic use are listed under the reimbursed group A-37. Under chapter VI alinea 3 the radioisotopes for diagnostic use are given under reimbursed group B-205. The reimbursement differs between diagnostic and therapeutic use radioisotopes. For diagnostic use the amount of reimbursement is defined by the type of radioisotope or the type of labeling of the radioisotope (see also appendix 2). Radioisotopes have to follow a reimbursement procedure under the RIZIV/INAMI Commissie Tegemoetkoming Geneesmiddelen/ Commission Technique du Médicament with the "Technische Raad voor Radioisotopen / Conseil Technique des Radioisotopes" according to the law of 27 December 2005. The composition of this council was only recently defined, in Royal Decree of 28 December 2006. The council is composed of members of the health insurance companies, medical specialists in radiotherapy, nuclear medicine and hospital pharmacy, a member of the Federal Agency for Nuclear Control (FANC/AFNC), a representative of the Ministry of Social Affairs and one of the Ministry of Public Health and one member of RIZIV/INAMI. The Committee's task is to advice the Insurance Committee on interpretation rules for the national reimbursement schedule (nomenclature). The members of the council have however not yet been nominated, thus prolonging the legal uncertainty.

The amount invoiced for radioisotopes for therapeutic use is fully covered by the health insurance. Only for the use of ^{125}Iodide and ^{103}Palladium the clinical indications have been restricted. For ^{90}Yttrium chloride solution approval by the sickness funds is required. The producer or distributor can thus freely set the price and sends the invoice to the hospital. The hospital then transfers the invoice to the health insurance without any control step. For a source used in multiple patients the invoice is sometimes split over the patients treated with the same source.

2.2 EVOLUTION OF REIMBURSEMENTS OF RADIOISOTOPES

Radioisotopes alone or molecules labelled with these were used in ± 570,000 scintigraphies or tomographies every year at a cost of 19.4 millions of EUR in the year 2000. The figure 1 indicates a slight increase of the expenditures in the years 2004 and 2005 to 20.7 millions of EUR. The evolution of the reimbursements of the radioisotopes for therapeutic use is instead worrying since the budget almost trebled within the last four years, from 1.73 millions in the year 2001 to 6.78 millions in 2005.

Figure 1: Evolution of reimbursements for radioisotopes from 2001 to 2005



2.3 EXPENSES FOR DIAGNOSTIC USES

Diagnostic radioisotopes for *in vivo use* are used by nuclear medicine specialists exclusively. These products are used as imaging agents for different scintigraphic procedures: Planar, sequential, whole body, single photon emission computed tomographies (spect) with or without whole body scintigraphy, double tomographies and positron emission tomographies. Several radioisotopes can be used for a same kind of scintigraphy and conversely a single isotope can fit different imaging procedures. Both the radioisotope and the procedure are reimbursed. The reimbursement codes for these diagnostic radioisotopes are generic in that sense that a same code can be used for up to 4 different isotopes or serves for many different labelling with a single radioisotope like ^{99m}Tc.

Radioisotopes for diagnostic use

All radioisotopes used for diagnostic purposes qualify for reimbursement. The reimbursement basis is a fixed fee, defined per radioisotope, in the nomenclature (Table 1). Ambulatory patients pay a co-payment for the radio-isotopes used. The amount or percentage of co-payments is defined by law and depends on the patients' social statute.

Table 1: Fixed fees for radioisotopes for diagnostic use

Radioisotope	Fee in €
$Na^{131}I$ and $Na^{125}I$ (699016-699020)	4.96
Inorganic molecules ready for use (699031-699042)	9,92
(In)organic molecules labeled with short-living eluate (699053-699064)	18,59
Blood cells or plasma proteins labeled ex-vivo with an inorganic molecule (699075-699086)	24,79
Organic molecules ready for use (699090-699101)	29,75
(In)organic molecules labeled with short-living eluates produced by a generator (699112-699123)	37,18
^{123}I used in cases where the exploration of the thyroid in a previous exam delivered insufficient information, such that an additional examination with ^{123}I is appropriate* (699134-699145)	49,58
^{123}I used for the exploration of biliary atresia in paediatrics* (699156-699160)	49,58
^{123}I used for the exploration of a renal graft* (699171-699182)	49,58
^{111}In, ^{67}Ga and ^{201}Tl (699193-699204)	49,58
Radio-isotopes with low atomic weight, to say ^{15}O, ^{13}N, ^{11}C, ^{18}F used for Positron Emission Tomography, performed in the context of an act defined by nomenclature codes 442971 – 442982 for which an authorisation has been obtained from the advisory medical doctor of the insurance institute (699215 699226)	173,53
Ioflupane (DATSCAN ®) ^{123}I, used for single photon emission tomo-scintigraphy using a gamma-camera equipped with a high resolution collimator, with the window set to register the total absorption peak at 159 keV, if this examination has been prescribed by a specialist in neurology or neuropsychiatry, to detect a loss of functional dopaminergic neuronal terminations in the striatum area in patients with a clinically uncertain Parkinson syndrom if all of the following criteria have been fulfilled simultaneously: 1. the examination has never been reimbursed yet according to current reimbursement rules in this patient; 2. it concerns an adult patient and the examination is meant to make a differential diagnosis between essential tremor and Parkinson syndromes; 3. the medical doctor, specialised in neurology or neuropsychiatry, declares that anamneses and clinical examination are insufficient to make a differential diagnosis; 4. the maximum reimbursed dose is 1 vial of 2,5 ml or 185 MBq. An elaborate medical report from the neurologist or neuropsychiatrist, that confirms that all requirements for reimbursement are fulfilled, should be added to the bill of the individual patient as far as this has not already been done at the moment of charging. This report should be sent to the counselling doctor of the insurance organism (699230-699241).	749,11

* If ^{123}I is used for other purposes than those mentioned in this table, the radioisotope will be reimbursed on the basis of €9,92 or €29,75 depending on whether it concerns inorganic or organic molecules labelled with ^{123}I.

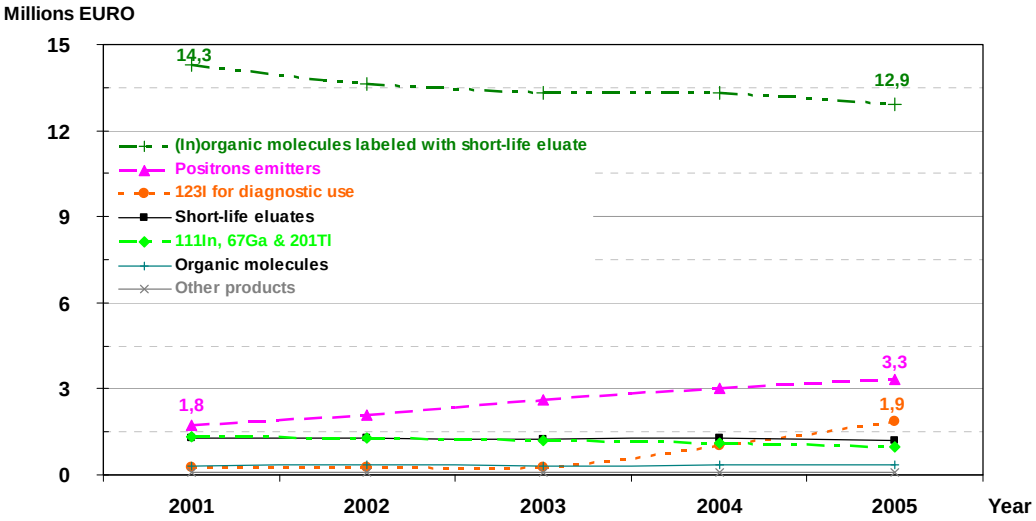
The evolution of the expenditures for diagnostic radio-isotopes shows that for most radioisotopes the expenditures have slightly decreased in the last 5 years (Table 2 and figure 2). Within the group of ^{111}In, ^{67}Ga and ^{201}Tl, the latter remains the most used.

The expenditures for ^{18}F, a positron emitter, and more recently for ^{123}I in the exploration of a doubtful Parkinson's disease show a sustained growth. The number of investigations for suspicion of Parkinson's disease is probably higher than the expected number of cases diagnosed every year.

Table 2: Evolution of the number of reimbursed diagnostic radioisotopes

	2000	2001	2002	2003	2004	2005	05/00
PLAN/SPECT							
Molecules labelled with short-lived generator produced radionuclide	445.747	448.424	428.777	421.250	422.673	411.608	- 7.7%
Unmodified organic or non-organic short-lived elutates from generators	83.543	84.298	84.190	83.836	84.787	81.110	- 2.9%
^{111}In, ^{67}Ga or ^{201}Tl	33.430	30.703	29.424	27.749	25.952	22.477	-32.8%
Organic molecules ready for use	13.154	12.779	13.451	13.180	13.796	14.691	11.7%
Use of ^{123}I after inconclusive thyroid exploration	6.902	6.703	6.869	6.395	6.169	5.448	-21.1%
Inorganic molecules ready for use	5.722	5.911	5.913	5.359	5.554	4.627	-19.1%
Na^{131}I and Na^{125}I	2.238	2.303	2.380	2.151	2.020	2.873	28.4%
^{123}I for exploration of a clinically doubtful Parkinson syndrome	0	0	0	0	1.041	2.194	>100%
Blood elements or proteins labelled ex-vivo with inorganic molecules	1.600	1.559	1.511	1.612	1.792	1.792	12.0%
^{123}I for the exploration of a renal graft	162	146	136	120	120	126	-22.2%
Suspension of ^{90}Y	147	155	129	156	103	69	-53.1%
Total number of reimbursed radioisotopes	592.645	592.981	572.780	561.808	564.007	547.015	- 7.7%
Positrons Emitters							
^{11}C, ^{13}N, ^{15}O, ^{18}F	7.608	10.517	12.518	15.765	18.285	20.140	165%

Fig. 2: Expenses for diagnostic radioisotopes from 2001 to 2005



2.4 EXPENSES FOR THERAPEUTIC USES

Reimbursement rules

Since 1988, reimbursement of radioisotopes for *therapeutic use* is based upon the presentation of invoices for ordered radioisotopes by the hospitals to the RIZIV/INAMI. The amount of the invoice is entirely reimbursed by the RIZIV/INAMI. There is no co-payment by the patient.

The radio-isotopes used are first charged by the producer to the hospital, who then charges the RIZIV/INAMI using one of the fourteen pseudo-billing codes for radio-isotopes. Some codes apply to more than one radio-isotope. For example, code 698110 applies to ^{182}Tantalium, ^{192}Iridium and ^{198}Gold -wires.

In 2001 the conditions for the reimbursement of radioisotopes for therapeutic use were defined by law (Royal Decree of 21 December 2001[a]). Two types of restrictions are imposed. First, only the radioisotopes that figure on a limitative list qualify for reimbursement (list in appendix). Second, for some radioisotopes reimbursement is conditional upon the disease or diagnosis of the patient. For example, ^{125}I and previously ^{103}Pd are only reimbursed for patients with prostate carcinoma stage T1-T2 with a PSA level below 20, Gleason score below 8 and prostate volume below 50 ml. Similarly, the reimbursement of solutions of ^{90}Y for the radioactive labelling of the pharmaceutical specialty Zevalin is conditional upon the simultaneous request for reimbursement of Zevalin and upon specific characteristics of the patient.

Expenditures for therapeutic radioisotopes

Therapeutic radioisotopes can be used either by physicians specialist in nuclear medicine and in radiotherapy. In number of procedures, the specialists in Nuclear Medicine are the main prescribers since the treatment of thyroid disorders and thyroid cancers represented in the year 2005 5 978 out the 9 665 therapeutic procedures. However, in value, this represented only 0.71 millions of EUR or 10% of the budget (table 3). ^{125}I was, by far, the main driver of the expenditures since it accounted for 5.12 millions of EUR or 75.6% of the total expenses in 2005 (table 4 & figure 3).

Table 3: Radio-isotopes for therapeutic use in 2005

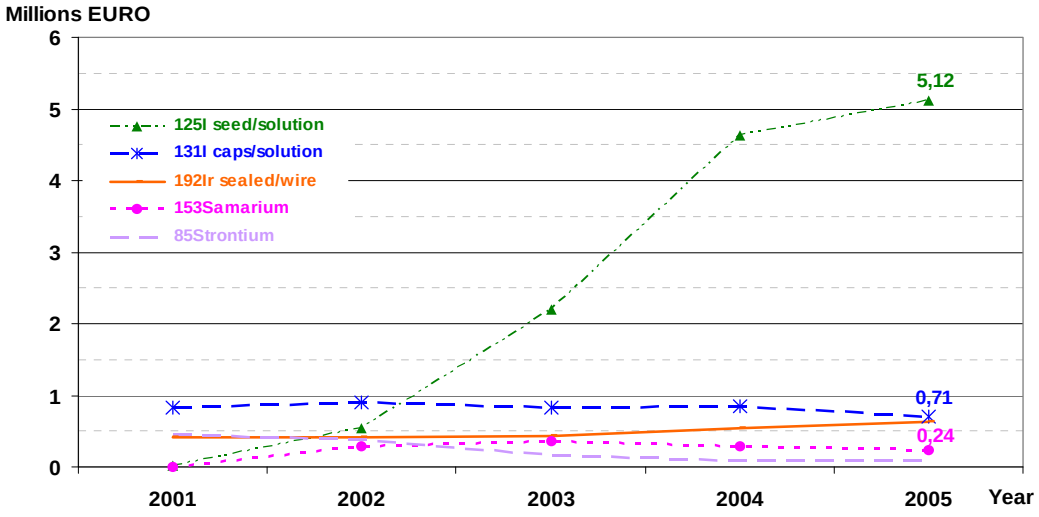
Tarification code	Description	Times charged (RIZIV data)
698051-698062	Sealed sources of ^{192}Iridium for therapeutic	267
698110-698121	Wires of ^{182}Tantale, ^{192}Ir and ^{198}Au	549
698132-698143	Solution of ^{125}Iodide for therapeutic use	490
698154-698165	Solution of Na^{131}Iodide for therapeutic use	1 142
698176-698180	Na^{131}I in caps	4 836
698390-698401	Suspension of ^{90}Yttrium microscopic glass beads for palliative treatment of patients with metastatic liver cancer	69
698456-698460	Solution or powder of ^{85}Strontium chloride or ^{85}Strontium & ^{89}Strontium	62
698471-698482	Solution of ^{153}Samarium for therapeutic use	290
698515-698526	Brachytherapy with ^{125}Iodide seeds	1 470

[a] Royal Decree of 21 december 2001- "Koninklijk besluit tot vaststelling van de procedures, termijnen en voorwaarden inzake de tegemoetkoming van de verplichte verzekering voor geneeskundige verzorging en uitkeringen in de kosten van farmaceutische specialiteiten. Publication 29/12/2001 in the Official Gazette (*Belgisch Staatsblad/Moniteur Belge)*

Table 4: Expenses for the mainly used therapeutic radioisotopes in EUR

	2000	2001	2002	2003	2004	2005	05/00
^{125}I seeds for brachytherapy			397.668	1.938.481	4.133.282	4.590.400	>999%
Na^{125}Iodide solution	16,553	20.784	139.253	262.246	490.492	533.689	>999%
^{182}Tantale, ^{192}Ir and ^{198}Au wires	238,568	270.934	211.000	251.871	302.723	387.414	+ 62%
^{192}Ir seeds in sealed sources	145,858	151.931	201.219	178.125	239.605	238.550	+ 64%
Na^{131}Iodide caps	547,150	607,862	723,518	608,898	584,364	545,640	- 0%
Na^{131}I solution	264,186	219,162	169,916	228,717	270,143	163,390	- 38%
^{153}Samarium solution		1.303	285.948	356.002	290.204	236.440	>999%
^{89}Strontium	431,498	453.233	381.985	162.458	97.741	82.759	-81%
^{90}Yttrium suspension	33,940	35,163	24,593	18,674	13,995	12,856	- 62%
All isotopes for therapeutic use	1,677,753	1,760,371	2,535,101	4,005,471	6,422,548	6,791,136	+ 305%

Fig. 3: Expenses for therapeutic radioisotopes from 2001 to 2005



Key points

- **The increase in RIZIV/INAMI expenditures for radioisotopes in the last 4 years is mainly due to an increase in the expenditures for ^{125}I, a radioisotope used for the treatment of prostate cancer.**
- **The expenditures for diagnostic radio-isotopes decreased slightly during the last 6 years but expenses for positrons emitters more than doubled in that period.**

3 DETAILED ANALYSIS OF THE EXPENSES OF THERAPEUTIC RADIOISOTOPES IN BELGIUM

In the previous chapter we presented the aggregated data on volumes and expenditures as available from the RIZIV/INAMI reimbursement data per code of the nomenclature. The data showed that for some radio-isotopes, the situation has changed rapidly from 2001 onwards: higher volumes of use and higher total expenditures. In this chapter, we focus on these radio-isotopes and try to find an explanation for these observations. We will examine between-centre variability in prices charged for radio-isotopes and volumes of radio-isotopes used.

3.1 METHODS

INAMI-RIZIV: codes of medical fees and pseudo-codes of radioisotopes

To obtain an almost exhaustive view of the activity in the year 2005, we worked on the databases 2005 and 2006, since the last months of 2005 were booked in 2006.

- Doc P for codes 260654-260665 (urology: prostate brachytherapy), sorted by centre, ward, month.
- Doc P for codes 442013 to 442024 (radioisotopes for therapeutic use), sorted by centre, ward, month.
- Doc P for codes 442212 to 442245 (radioisotopes for functional tests), sorted by centre, ward, month.
- Doc P for codes 442396 to 442982 (nuclear medicine: scintigraphy & tomography), sorted by centre, ward, month.
- Doc P for codes 444113 to 444603 (radiotherapy: external irradiation, brachytherapy), sorted by centre, ward, month.
- Doc PH for pseudo-codes 698014 to 698526 (radioisotopes for therapeutic use), sorted by centre, ward, quarter.
- Doc PH for pseudo-codes 699016 to 699241 (radioisotopes for diagnostic use) sorted by centre, ward, quarter.

Federal Agency for Nuclear Control (FANC/AFCN): We received the monthly listings of delivered radioactive substances with date of transport, name & address of the consignee, type of radionuclide, number of parcels and total activity in MBq or GBq.

Most of these data (3 out of the 4 transporters) were only made available on paper support and were manually entered at the KCE during the year 2007. We discarded radionuclides used for industrial, scientific or medical 'in vitro' use. The remaining radioactive products were sorted by medical centre. Some hospitals had several facilities that were regrouped. It was thus possible to get a precise picture of the yearly ordered quantities for every form of any radionuclide in each hospital. Most of the centres worked with weekly standard orders for their diagnostic products like ^{99m}TC, ^{67}Ga, ^{111}In and ^{201}Tl. The activity was expressed in mCi in order to have a common unit of radioactivity for all centres.

Producers: Either list of customers with date of invoice and products ordered, but no financial details, or total amount of products sold in the year to Belgian customers.

Hospitals: copies of the invoices for ^{125}I seeds and ^{192}Ir (sealed sources and wires) when requested.

Nuclear medicine specialists: our proposal of a national survey to learn what types of radioisotopes or labeled molecules were used in conjunction with what kind of diagnostic imaging procedures by organ or function was submitted to the President and 2 representatives of the Belgian Society of Nuclear Medicine (Drs S. Goldman, M. Dusart & P. Paulus for BELNUC,) in May 2007. These gentlemen refused to support the initiative of the KCE without knowing the true purpose(s) behind the survey organized by our institution. The KCE has no hidden agenda, but they refused to go further.

A similar initiative directed to the Professional Association of Specialists in Nuclear Medicine, a branch of the Belgian Specialists Association (VBS-GBS) was also rejected by its president, L. Kiebooms, as extremely tedious for the members of his Association.

The Table 5 gives an overview of the different data sources we used and their respective contents.

Table 5: Cross-table for the analysis of radioisotopes

	FANC data	Producers data	Hospital or centre	RIZIV code	INAMI pseudocode*
Diagnostic use					
Place of use	+	+	-	+ (ward)	+ (ward)
Date of delivery	+	±	-	Monthly	Quarterly
Radionuclide	+	+	-	-	±
Total activity	+	±	-	-	-
Value of goods in €	-	-	-	+	Sum/quarter
Therapeutic use					
Place of use	+	+	-	+ (ward)	+ (ward)
Date of delivery	+	±	-	Monthly	Quarterly
Radionuclide	+	+	-	+	+
Total activity	+	±	-	-	-
Invoiced goods in €	-	-	+ if requested	+	Sum/quarter

* Pseudo-code: up to 4 different radionuclides can be included in a pseudo-code

3.2 RESULTS

3.2.1 Brachytherapy

Brachytherapy is a type of radiotherapy that places radioactive sources in or adjacent to target tissues. The main tumor sites are gynaecology, prostate, breast, bronchus and head and neck. There are two main types of brachytherapy:

Temporary seed loadings where the sources are placed in catheters, needles, or other appliances for a brief period of time, then removed.

Permanent seed implants where the radioactive seeds are left in the tumor as commonly used for the treatment of prostate cancer.

The goal is the same - to conform the radiation dose to the size and shape of the target and limit the side effects by sparing the surrounding healthy organs. Since the sources are placed in the target area, the technique takes advantage of the inverse square law (the intensity of radiation is reduced by the square of the distance from the source) to achieve the goal.

HDR Brachytherapy

High-dose-rate (HDR) brachytherapy is a technique that uses a relatively intense source of radiation—typically a 10 Curie source made of ^{192}Iridium—to deliver a therapeutic dose of radiation through temporarily placed needles, catheters, or other treatment appliances, known as applicators. Thirteen centres propose HDR with 10-12 Ci sources. Since ^{192}Iridium has a half-life of 74 days, the sources must be replaced every 3 to 4 months depending of the initial radioactivity: When a 12 Ci source is employed, the residual activity after 4 months comes to 4.0 Ci. If a 10.6 Ci source is used, the activity at the end of a quarter is equal to 4.5 Ci.

The source is usually attached to a cable. This cable extends from a shielded container into an applicator using a stepping motor to control the channel used, the distance(s) at which the source stops, and the length of time that it dwells there.

By varying the position and dwell time, the dose can be neatly sculpted to provide a dose geometry which conforms to the shape of the target. The total dose is typically delivered in a series of two to ten fractions, or treatment sessions.

The computer controlled afterloader technique provides significant advantages over older, manual loaded brachytherapy techniques: Prospective treatment plans are performed after applicator placement but before radiation delivery. The computer controlled stepping of the source permits a precise shaping of the dose distribution, to destroy the target tissue while sparing as much healthy tissue as possible. The high dose delivery supports a rapid, more patient friendly, out-patient treatment. Traditionally, HDR brachytherapy has been used to treat cancers of the cervix and endometrium, bronchus, esophagus, head and neck, and soft tissue sarcomas.

PDR Brachytherapy

Pulsed-dose-rate (PDR) brachytherapy is similar to HDR, but radiation is delivered in short 'pulses' over several hours or days. The source used is typically a 1-2 Curie ^{192}Iridium source, assembled and driven in the same way as HDR.

This technique has the primary advantage that it is biologically similar to traditional low dose rate (LDR) techniques where sources are manually loaded into catheters and applicators and left in place for several hours to days. However, PDR adds the remote controlled afterloader advantages of radiation safety, prospective planning, and precise dose shaping.

Unlike the HDR technique, PDR treatments are delivered on an in-patient basis and require a dedicated shielded treatment room where the patient can stay for up to three days. Control of applicator movement during that time is also required. To support patient care during the course of treatment, PDR equipment typically has a treatment interrupt facility to help ensure that the radioactive source will not be deployed while nurses, hospital staff, and visiting family members are in the room.

Many treatment centers prefer the PDR technique for treatment where contact with mucosa is involved—especially for gynecological treatments. Seven centres offer PDR therapy with sources of 1-2 Ci ^{192}Ir.

Permanent prostate brachytherapy

Prostate brachytherapy is another form of LDR brachytherapy only indicated for the treatment of early stage prostate cancer. In this technique, radioactive 'seeds' about the size of a grain of rice are positioned in the prostate using needles that are guided into position by ultrasound and a template or grid through which the needles are inserted to control their spacing (figure 4).

The challenge is to place the seeds so the radiation dose adequately covers the entire prostate, but spares as much surrounding tissue as possible. To accomplish this task, the radiotherapist needs the help of a sophisticated treatment planning system, which uses 3-dimensional trans-rectal ultrasound images as illustrated in figure 5 to help design the intended placement of sources, and then provides ‘dynamic dosimetry' to update the dose map in real time during the deposition of the individual seeds in the prostate.

Figure 4

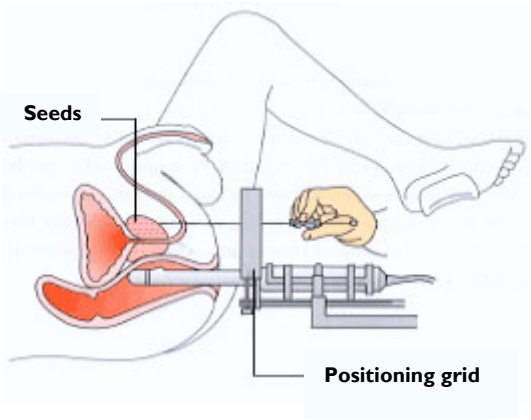
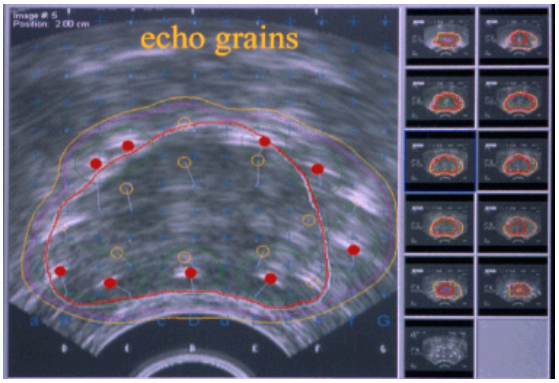


Figure 5



This allows the physician to compensate in real time for any gaps that may arise as a result of prostate deformation by the needles, or other needle placement issues that may occur. The same software can also extract seed images from a post implant computed tomography image set to confirm the received dose distribution.

It is common to place ± 2 seeds per cm^3 of the gland. The volume to be treated varies from 20 to a maximum of 50 ml. So from 50 to 100 individual seeds may be placed in a single session. Radiation is then delivered to the prostate slowly over the 13 following months (what means for ^{125}I a residual activity of 1% at the end of this period). Most of the ^{125}I seeds used in Belgium were from IBt/Tyco Healthcare Belgium/Bard Benelux, Amersham/Oncura/General Electric, and Eckert & Ziegler/Belgium Medical. Seeds are sold by piece and by 10-seed strand. Radioactivity of the seeds at reference time varied from 0.383 to 0.489 mCi and from 0.32 to 0.50 mCi respectively for Amersham/Oncura and for IBt/Bard.

3.2.2 ^{192}Iridium sealed source and wires

^{192}Ir treatment with sealed source

The choice of the correct code represents clearly a challenge for most of the centres. The pseudo-code 698051–698062 covers the utilization of ^{192}Iridium seeds contained in sealed containers, what clearly means that they are never in direct contact with the patient's body: these sources move inside a catheter placed in the close vicinity of the tumor. The same pseudo-code is applicable for HDR and PDR therapy with ^{192}Iridium. Instead of this code, 11 out of the 14 centres applied the code for ^{182}Tantale, ^{192}Ir and ^{198}Au wires. It is therefore more appropriate to consider the existing code for "brachytherapy with automatic projection of a radioactive source in the patient" (code 444555-444566). The table 6 shows the number of medical fees for "automatic projection" and the number of times the correct pseudo-codes were billed. The great majority of hospitals did not use that pseudo-code but the pseudo-code for the wires.

Table 6: Use of High Dose Rate and Pulse Dose Rate brachytherapy

Hospital	444555	44456	HDR	698051	698062	^{192}Ir
Middelheim Antwerpen	6	24	30	6	Unknown*	Unknown
St Joseph & Thérèse Gilly	40	6	46	60	3	63
St Maarten Duffel	30	1	31			
St Jan Brugge	45		45			
St Elisabeth Turnhout	41	42	83			
Bordet Brussels	62	32	94		4	4
St Augustinus Wilrijk	24	206	230	Unknown	Unknown	Unknown
St Jean Brussels	5	2	7			
Deux Alice Brussels	21		21			
OLV Aalst	22	1	23	81	Unknown	82
VUB Brussels	13	6	19			
Jolimont	43	9	52			
St Elisabeth Namur	12	41	53			
Virga Jesse		64	64			
St Lucas Gent		36	36			
KUL Leuven	8	82	90			
Vésale Montigny	25	3	28	Unknown	Unknown	Unknown
Cavell Brussels		43	43	Unknown	Unknown	Unknown
Groeninghe Kortrijk		2	2			
RUG Gent		36	36		50	50
Sart Tilman Liège	202	62	264		Unknown	Unknown
All 21 hospitals	599	698	**1.297**	147	58	**205**

Unkown*: the aggregated invoices obtained from INAMI/RIZIV did not allow to identify the individual cases.

The cost per source fluctuated between €3 323 and €8 137, for 1 Ci as well as for 12 Ci.

The centres have developed different ways to share the costs:

- The cost of the source was divided amongst the number of attendees during the period of utilization;
- The total cost of the sources bought during that year was divided amongst 10 attendees in that year (at random ?)
- The cost of the source was divided amongst the first 12 or 20 patients, then 0 € for the next patients;
- The cost of the source was charged on the first patient, then 0 € for all the next patients.

At least one hospital charged more than the total cost of the sources bought in the year 2005. Some centres included other costs like a cable or their service contract. Large hospitals had 2 or even 3 HDR/PDR devices and so the cost of the 2 or 3 sources per quarter are perfectly legally charged to the INAMI-RIZIV.

Table 7: ^{192}Ir treatment with sealed source (HDR or PDR) in 2005

Centre	HDR	PDR	444555 444566	Pseudo-codes billed	Mean cost
Middelheim Antwerpen	+	-	30	6	€ 927
St Joseph & Thérèse Gilly	-	+	46	63	€ 285
St Maarten Duffel	+	-	31	31	€ 449
St Jan Brugge	-	-	45	0	
St Elisabeth Turnhout	+	-	83	4	€ 4 051
Bordet Brussels	+	-	94	19	€ 189
St Augustinus Wilrijk	+	+	230	12	€ 8 137
St Jean Brussels	+	-	7	3	€ 1 197
Deux Alice Brussels	+	-	21	21	€ 601
OLV Aalst	+	-	23	82	€ 225
VUB Jette	+	-	19	0	
Jolimont Haine St Paul	+	-	52	71	€ 150
St Elisabeth Namur	-	+	53	52	€ 288
Virga Jesse Hasselt	-	+	64	55	€ 469
St Lucas Gent	-	+	36	4	€ 4 122
Gasthuisberg Leuven	-	+	90	0	
Vésale Montigny	+	-	28	77	€ 437
Cavell Brussels	-	-	43	Unknown	Unknown
Groeninghe Kortrijk	-	-	2	0	
RUG Gent	++	+	36	50	€ 755
Sart Tilman Liège	+	-	264	31	€ 259
All	13	7	1 297	581	

HDR: high dose rate (10-12 Ci/source); PDR: pulse dose rate (1-2 Ci/source)
444555 – 444566: number of fees paid to the radiotherapist per course of "automatic projection of a radioactive source in a patient" (€114.65)
Pseudo-codes: number of patients charged for the use of ^{192}Ir sealed source (whatever the pseudo code used) with the mean cost in that centre.

^{192}Ir treatment with wires

All the 14-cm wires were manufactured by Canberra which applied the same tariff for the 14 centres. The cost depends of the number of wires bought; the price is the same for a broad range of radioactivities. The cost per patient started at €369.50 for half a wire to €2873 for 5 wires.

The wires were billed under the wrong code (698051-698062) in 3 hospitals and under the correct one (698110-698121) in the 11 other hospitals. But the content of the pseudo-code 698110-698121 was polluted by the numerous miscoding of HDR/PDR.

3.2.3 ^{125}Iodide seeds and solutions

There were several ways to analyze the number of brachytherapies performed in Belgium. The most obvious one was to take the code 260654-260665 specific for the urologists; this figure should faithfully reflect the number of brachytherapies done in that year. We found 950 reimbursed interventions in 2005 (table 6). However, the number of reimbursements granted for the ^{125}I seeds, 1470, was far higher than the number of interventions performed. Some delay in the introduction of the claims either by the urologists or by the hospitals for the iodide seeds bought could explain a small discrepancy between the 2 numbers but not to such an extent. A detailed analysis of the reimbursed amounts delivered astonishing results. Some aggregated invoices included up to 150 bills for trivial amounts:

St Jan Brugge (710049) Q I: 115, Q II: 45 & 20, Q III: 65, Q IV: 55 & 20

St Trudo St Truiden (710715) Q I: 70

ZOL Genk (710371) Q I: 19, Q II: 43 & 14, Q III: 95, Q IV: 150

One of the producers of the iodide seeds was contacted and assured us that these invoices could impossibly correspond to that impressive number of patients.

In few cases, we found also that the amount accounted was to high for the number of invoices: Klina Brasschaat (71071009) Q IV: 5 invoices for a total of €75 938.20

It was then decided to collect the invoices for the seeds bought by the hospitals when the aggregated quarterly bills received by the INAMI-RIZIV did not allow to individualise the cost of the iodide seeds by patient. We requested these hospitals to erase any identification of patient's name. Almost all contacted hospitals sent us voluntary these documents without delay.

These documents, with the proof of ^{125}I deliveries from the AFCN-FANC, also permitted us to identify brachytherapies miscoded. The table 8 sums up the many cases founded as well as the recalculated number of reimbursed procedures.

Table 8: Correspondence between brachytherapy, urologist fee and radiotherapy

Hospital	Radiotherapist		Urologist		^{125}I seeds	
	444253	444264	260654	260665	698515	698526
Gasthuisberg KULeuven	4	23		20		10
Sart Tilman Liège	55	23	42	48	30	31
Groeninghe Kortrijk		81		83	2	78
St Augustinus Wilrijk	17	48		30		29
Salvatore-St Ursula Hasselt		2		22		20
UCL St Luc Brussels	3	71	2	29		
I. Bordet Brussels	11	19		4		
ULB Erasme Brussels		10		15		9
Edith Cavell Brussels		28		21		1
ZOL Genk		22		22		18
St Elisabeth Turnhout	6	42		48		37
Clin Europe Brussels	4	53		53		48
St Jan Brugge	10	72		82		64
St Lucas Gent		49		47		
Virga Jesse		25	0	27		27
H Hart Roeselare	4	23		24	4	18
St Dimpna Geel		23		23		16
Klina Brasschaat		22		22		22
St Jean Brussels	2	28		25		16
St Lucas/Jozef Brugge		24		25		24
St Maarten Mechelen	9	29		28		27
OLV Aalst	2	19		18		14
St Elisabeth Namur	33	10		27	22	
St Jozef Malle		24		24		22
OLV Waregem		2		4		4
Jan Palfijn Merksem				33		27
St Jozef Izegem				2		2
St Trudo St Truiden		21	2	21	1	9
Stedel. Roeselare				1		1
Imelda Bonheiden		29		31		25
Heusden-Zolder		14		14		12
Jolimont/Nivelles	8	10		7		
Vésale Montigny/le/Tilleul	20	23		5		
HH Leuven	1	2	4	3		1
St Elisabeth Zottegem		6		6		5
St Andries Tielt				2		1
OLV Waregem						4
Jan Palfijn Gent				4		
All the 38 centres	189	877	50	900	55	613

Table 9: Number of prostate brachytherapies actually reimbursed in 2005

	Ambulatory	Hospitalized
According to INAMI-RIZIV:		
698515-698526 (^{125}I seeds)	152	1318
260654-260665 (urologist)	50	900
After review of the invoices:		
698515-698526 (^{125}I seeds)	55	613
698132-698143 (^{125}I solution)	2	74
698110-698121 (^{192}Iridium wires)	4	6^{+} (<14)
698471-698482 (^{153}Samarium)	0	11
True total reimbursed	**61**	**704^{+}**

These different elements clear up the "brachytherapy" landscape: starting from the number of reimbursed urologists fees (950), we can conclude that not all the treatments with radioactive seeds were reimbursed either the case did not correspond to the prescribed rules for a reimbursement, or the invoices have not yet been transmitted to the INAMI-RIZIV.

Reimbursement rules

The reimbursement by the INAMI-RIZIV is authorized within the following specific rule: "treatment of local prostate carcinoma of stage T1-T2, with a prostate specific antigen (PSA) plasma level lower than 20 ng/ml, a Gleason score lower than 8 and a prostatic volume lower than 50 ml" and must be submitted to the medical adviser of the patient's sickness fund.

Cost of the seeds

All the therapeutic pseudo-codes reimbursed by the INAMI-RIZIV to every hospital were reviewed whatever the corresponding therapeutic isotope and then disaggregated per patient. We paid a special attention to unusually high reimbursements under other pseudo-codes than for ^{125}I seeds.

The cost of seeds is estimated in two ways:

The first way gives the mean cost per patient. It is obtained for every hospital by dividing the sum of the invoiced seeds received in that hospital by the number of patients treated locally as presented in table 10. The median cost was €6 890.00.

The second way consisted to request and then to analyze the invoices received by the hospitals. In the majority of the centres, a flat price was charged irrespectively of the number of seeds needed.

A distributor systematically adapted the cost per strand in its "invoices" in order to always get the same final price as shown in table 11. However, the message was not perfectly understood by the computer that made the invoices (see last column).

Table 10 : Mean radioactivity, mean number of seeds per patient, and mean reimbursement by the INAMI-RIZIV in the year 2005

Hospital	Number of patients*	Mean activity	Seeds per patient	Mean reimbursement
Gasthuisberg KULeuven	18	35.4 mCi	85.6**	€4955.50
Sart Tilman Liège	68	32.6 mCi	93.3	€4970.28
Groeninghe Kortrijk	71	Unknown	80.8	€6890.00
St Augustinus Wilrijk	29	32.8 mCi	79.3	€6483.90
Salvatore-St Ursula Hasselt	20	35.5 mCi	83.0	€6163.90
UCL St Luc Brussels	27	37.1 mCi	74.4	€6532.80
I. Bordet Brussels	1	37.8 mCi	84.0**	Unknown
ULB Erasme Brussels	9	Unknown	82.6	€6890.00
Edith Cavell Brussels	24	33.0 mCi	79.9	€4295.41
St Elisabeth Turnhout	37	35.6 mCi	76.0	€5065.65
Clin Europe Brussels	48	32.2 mCi	80.6	€5102.16
St Jan Brugge	64	Unknown	84.5	€6890.00
St Lucas Gent	47	27.5 mCi	71.9	€6328.20
Virga Jesse Hasselt	27	30.6 mCi	73.9	€7060.74
H Hart & Stedelijk Roeselare	30	35.3 mCi	77.5	€6890.00
St Dimpna Geel	16	Unknown	82.8	€6890.00
Klina Brasschaat	22	30.3 mCi	73.8	€6328.17
St Jean Brussels	22	Unknown	83.9	€6890.00
St Lucas/Jozef Brugge	24	Unknown	82.7	€6890.00
St Maarten Mechelen	9	Unknown	84.2	€6328.19
OLV Aalst	14	29.1 mCi	64.7	€6177.15
St Elisabeth Namur	22	31.8 mCi	79.6	€4253.71
St Jozef Malle	22	Unknown	84.2	€6890.00
OLV Waregem	4	Unknown	85.0	€6890.00
Jan Palfijn Merksem	27	Unknown	84.2**	€6890.00
St Trudo St Truiden	10	28.1 mCi	68.0	€6312.30
Imelda Bonheiden	25	Unknown	82.4	€6890.00
Jolimont/Nivelles	11	38.3 mCi	100	€5692.91
Vésale Montigny/le/Tilleul	8	37.3 mCi	95.0	€6457.35
HH Leuven	6	28.7 mCi	75.0	€6328.20
St Elisabeth Zottegem	5	Unknown	82.5	€6890.00
OLV Waregem	4	Unknown	85.0	€6890.00
Median for the 31 centres			**80.8**	**€6890.00**

Number of invoices with enough information available; we have received more invoices than the number of treatments with code 698515-698526

** Data from the manufacturer

Table 11 : The Oncura «flat price »

# of strands	Cost / strand(VAT excl.)	Final cost(VAT inclusive)
6	€995.00	€6 328.20
7	€852.85/86	€6 328.15/22
8	€746.25	€6 328.20
9	€663.33	€6 328.17
10	€597.00	€6 328.20

An other distributor, Bard, systematically charged a flat price of €6 890.0 corresponding to 130 seeds at the official price of IBt, its producer, but concealing in its "invoices" the number of seeds shipped as well as their specific radioactivity and incorporating the hidden cost of the treatment planning system.

A minority of centres ordered the number of seeds corresponding to the therapeutic needs of the individual patients. Table 12 shows the costs applied by the 3 producers and their distributors.

Table 12 : Cost of goods according to the number of seeds, VAT inclusive.

# seeds	IBt direct	IBt through Tyco Healthcare	IBt through BARD
50	€2 491.00	€2 491.00 - 2 650.00	€2 491.00
60	€2 989.20	€2 989.20 - 3 180.00	€2 989.20
70	€3 487.40	€3 487.40 – 3 710.00	€3 487.40
80*	€3 985.60	€3 985.60 – 4 240.00	€3 985.60
90	€4 483.80	€4 483.80 – 4 770.00	€4 483.80
100	€4 982.00	€4 982.00 - 5 300.00	€4 982.00
Flat price	No invoice	**€6 532.80**	**€6 890.00****
# seeds	**Amersham direct**	**Amersham through Oncura**	**Eckert & Ziegler through Belgium Medical*****
50	No invoice	No invoice	€2 491.00 - 4 770.00
60	€3 975.00	€3 796.92 - 3 975.00	€2 989.20 - 5 724.00
70	€4 637.50	€4 429.74	€3 487.40 - 6 678.00
80*	€5 300.00 - 8 013.60	€5 062.56	€3 985.60 – 7 632.00
90	€5 962.50	€5 695.38 - 5 962.50	€8 586.00
100	€5 565.00 - 6 328.20	€5 565.00 - 6 328.20	No invoice
Flat price	**€6 010.20 - 6 328.20**	**€6 328.20**	No invoice

* Median number of seeds implanted in the centres listed in table 10 for the year 2005.

** Flat price for a package of the same seeds as sold by IBt SA, but inclusive the software needed for a correct application of the seeds.

*** Most of the seeds were delivered as individual seeds but occasionally a part of the delivery included 2 strands of ten seeds priced with a 17% surcharge.

The interstitial brachytherapy in France

Table 13: Distribution of implanted ^{125}I seeds for the treatment of prostate cancer.

	Min	**Mean**	Max	σ
Lyon	49	**75.7**	102	12.0
Paris	37	**75.7**	117	16.4
Nancy	43	**76.2**	123	15.4
Toulouse	49	**71.9**	96	11.5
Poitiers	55	**81.1**	129	17.0
Marseille	64	**93.2**	129	13.4
All (305 pat.)	37	**80.0**	129	16.4

Livartowski, 2004, Evaluation médico-économique de la curiethérapie dans le cancer localisé de la prostate comparée à la prostatectomie radicale et à la radiothérapie externe: rapport à 12 mois.

The interstitial brachytherapy in The Netherlands

In Maastricht, it is usual to place a mean of 80.0 seeds at an individual cost of €42.50, VAT excluded.

The actual cost charged to the INAMI-RIZIV for a mean of 80 seeds per prostate is thus without correspondence with the market price for the number of seeds really ordered neither in Belgium, nor in other countries.

Cost of the procedure

A prostate brachytherapy requires that the radiotherapist assists the urologist during the intervention in order to balance the radiations delivered by the seeds. The fees include:

the full reimbursement of the implanted ^{125}I seeds as decided by the radiotherapist (median charge of 6 890.00 EUR with code 698515 - 698526),

the medical fee for the urologist when the radioactive material is inserted in the prostate (294.87 EUR with code 260654-260665),

the fees for the radiotherapist, to say a "lump sum for brachytherapy exclusively", a fee for the "preparation and treatment simulation" and a fee for the "calculation of the dose distribution" (respectively 1375.80 EUR, 343.95 EUR, 286.63 EUR with codes 444253-444264, 444356-444360 and 444393-444404).

The median cost for a prostate brachytherapy was €9191.25 in 2005.

Table 14 : The direct cost of prostate brachytherapy in 2005

^{125}I seeds	Urologist	Radiotherapy
€6 890.00 (median)	€294.87	€1 375.80 €343.95 €286.63

Cost of maxi-forfait if daycare or 1-day hospital stay and anesthetist and theatre are not included

3.2.4 ^{131}Iodide caps and solutions

Table 15: Mean cost and number of patients treated with ^{131}Iodine.

^{131}Iodine caps	**Patients**
€85.77	Ambulatory (3 495)
€212.63	Hospital (927)
^{131}Iodine solution	
€70.77	Ambulatory (771)
€148.4	Hospital (217)
MIBG-^{131}Iodine solution	
Not applicable	Ambulatory (0)
€3336.13	Hospital (8)

Jan Yperman, Ieper and H. Serruys, Oostende excluded

3.2.5 ^{153}Samarium solutions

^{153}Samarium lexidronam (Quadramet®, Schering) is indicated for bone pain palliation in confirmed osteoblastic metastatic bone lesions at a dose of 1 mCi/kg weight.

The frequency and the mean cost charged are presented in table 16.

Table 16: Mean cost and number of patients treated with ^{153}Samarium.

^{153}Samarium	Patients
€1303.33	Ambulatory (87*)
€1356.34	Hospital (31)

Schering charged always an amount of €1 303.32 whatever the ordered activity (which obviously depended of the patient's weight since the dose is 1 mCi per kg)

*One hospital billed 72 and 70 invoices of respectively €18.10 and €18.62 for 2 ambulatory patients: these 2 patients are therefore accounted only for 2. An other hospital used the ^{153}Samarium code for ^{125}I brachytherapies of prostate cancer.

3.2.6 ^{89}Strontium

^{89}Sr-strontium chloride (Metastron®) for the treatment of bone metastasis

Table 17: Mean cost and number of patients treated with ^{85}Strontium.

^{89}Strontium	Patients
€1410.02	Ambulatory (35)
€1401.78	Hospital (11)

3.2.7 ^{90}Yttrium suspension

The suspension of uncoupled ^{90}Yttrium (Terasphere) is indicated in the treatment of hepatocarcinoma. It was used for 63 patients (21 ambulatory, 42 hospitalized) in 35 centres under the pseudo-code 698390-698401. The delivered activity varied from 8 to 118 mCi (mean 28 mCi) without related price differences.

One hospital charged 10 times the usual price for a patient treated but the delivered radioactivity was of the same magnitude as for the 2 other patients treated that year in the same institution.

Table 18: Mean cost and number of patients treated with ^{90}Yttrium.

^{90}Yttrium	Patients
€155.63	Ambulatory (21)
€174.51*	Hospital (42)

*Cost after adjustement for the above mentioned error.

^{90}Y Ibritumomab tiuxetan (Zevalin®) is indicated for the treatment of patients with relapsed or refractory low-grade, follicular or transformed B-cell non-Hodgkin's lymphoma, including patients with rituximab-refractory follicular NHL. However, the coding does not allow to know if there were some beneficiaries in the year 2005.

3.2.8 Conclusion

Key points

- **The application of the pseudo-codes for HDR/PDR is confusing.**
- **The calculation of the individual share in the cost of the ^{192}Ir HDR/PDR is complex and disadvantage the hospitals which spread their cost on all the patients of the quarter.**
- **The full coverage by the INAMI-RIZIV encourages the acquisition of a 2^{d} device in the large centres, the coverage of the spare parts via service contract and does not discourage the very small centres to offer that treatment.**
- **Many hospitals do not pay attention to a correct registration of the reimbursement for ^{125}I seeds. Thus, neither the number of prostate brachytherapies performed, nor their cost can be estimated on the basis of the pseudo-code for ^{125}I seeds.**
- **The different (pseudo)codes for brachytherapy are not submitted to the Insurer altogether for the reimbursement.**
- **The price charged by one distributor always included the cost of the treatment planning system.**
- **The actual cost of the procedure with a mean of 80 seeds per prostate is without correspondence with the market price for the number of seeds really ordered.**
- **The same distributor systematically concealed in its invoices the number of seeds shipped as well as their specific radioactivity.**
- **^{153}Sm was always charged at €1303.32 per patient, whatever the dose.**

4 INTERNATIONAL COMPARISON

4.1 INTRODUCTION

This chapter describes the use and reimbursement of radioisotopes for diagnostic and therapeutic use in a number of selected countries. The information in this chapter is largely based on grey literature as peer-reviewed literature on this subject is rare. A Medline, Embase and Econlit search revealed no single relevant English, Dutch or French article.[b]

To be able to understand the reimbursement of radioisotopes in a country, it is necessary to understand the general health care financing principles in that country. The description of the current health care financing systems in the different countries is primarily based on the information provided in the country reports of the *health*Basket Project (http://www.ehma.org/projects/default.asp?NCID=112). Specific information on the financing of radioisotopes has been collected through personal contacts.

No literature or other sources were found detailing the price structure of the radioisotopes for medical use.

This chapter is split into different parts. The first part provides some background information on the international market of radioisotopes. The second part compares the volumes of radioisotopes used in different countries. The third part describes the financing systems for radioisotopes in five countries, including Belgium.

The selection of the countries is based on the characteristics of their health care financing system and their proximity to Belgium. They include the Netherlands, France, Italy and the UK. The health care financing system in all four of these countries is either in transition or has been modified very recently. France and the UK are in different phases of transition to a per-case payment system and come from fundamentally different former financing systems. Given their different background, it is interesting to examine how they deal with the reimbursement of radioisotopes in their reforming system. Italy is characterised by a high level of decentralisation and high autonomy of the regions. The Netherlands has recently moved to a per-case payment system for hospital care. Since the system is already in use, it provides a useful example of how the financing of radioisotopes works in a per-case payment system.

4.2 PRODUCTION OF RADIOISOTOPES

4.2.1 World market

Worldwide, radioisotopes for diagnostic use account for 85.5% of the medical radioisotopes market; 9.5% of the isotopes produced is for therapeutic use and about 5% is for research purposes (mainly biomedical medical tracers). For diagnostic procedures, ^{99}Mo and PET isotopes are the most frequently used radioisotopes. They are responsible for more than 80% of the production volume, which implies a market share of 68.4% of the entire radioisotope production.[1]

Although the market share of therapeutic radioisotopes is much lower than the market share of diagnostic radioisotopes, the amount of money spent on therapeutic radiopharmaceuticals is relatively high due to the higher prices of therapeutic radiopharmaceuticals. About 20% of the turnover on the market of radiopharmaceuticals is for products that are used for therapeutic procedures.[2]

Radioisotopes are produced either in reactors or accelerators (cyclotrons). Reactors typically produce neutron-rich isotopes by neutron irradiation, whereas accelerators tend to produce neutron-deficient isotopes by proton, deuteron or alpha particle

[b] One potentially relevant reference in Japanese was found. None of the authors of this report, however, has mastered this language.

bombardment. Some radioisotopes can be produced in any of the two radioisotope production facilities. Examples include ^{97}Ru, ^{67}Cu, ^{186}Re and ^{99}Mo. [1]

Table 19 shows the number of radioisotope production facilities (reactors and accelerators used for radionuclide production) in a number of European countries, the US and Canada. The number of cyclotrons differs according to the source. A survey by the Joint Research Centre (JRC) of the European Commission[1] reported higher numbers of cyclotrons in most countries than a survey by the International Atomic Energy Agency (IAEA: IAEA Directory of Cyclotrons used for radionuclide production)[3]. The methods used in both surveys differed. The JRC survey relied on information provided by the members of the European Association of Nuclear Medicine (EANM), while the IAEA relied on information from "known institutions operating cyclotrons for radionuclide production". Besides the omission of "unknown" institutions in the IAEA survey, the difference in numbers of cyclotrons may also be explained by the inclusion of small low-energy and low current accelerator units in the JRC survey (van Velzen, personal communication). This cannot explain, however, the instances where the figure of the JRC is lower than the figure of the IAEA.

Table 19 : Number of reactors and accelerators in different countries as of January 2003

Country	Number of Reactors (pmp as of 1 January 2003)	Number of Accelerators (pmp as of 1 January 2003)[a 1]	Number of Accelerators (pmp as of November 2005)[b3]	Population (million)
Belgium	1	11	8	10.4
France	2	7	6	58.9
Germany	1	29	23	82
Italy*	1	9	13	57.3
Netherlands	1	8	10	16.2
Norway	1	1	1	4
Sweden	1	1	1	8.9
US	8	74	70	272.6
Canada	1	9	9	31

* according to a report of the Italian association of Nuclear Medicine, the number of accelerators in Italy was 22 in 2006.

[a] Source: van Velzen et al. 2003, DG JRC, Institute for Energy[1]

[b] Source: IAEA-DCRP/2006; Directory of cyclotrons used for radionuclide production in member states: 2006 update[3]

The growing demand for PET in recent years has increased the number of cyclotrons with more than 7% between January 2003 and November 2005.[3] The production of PET-radioisotopes requires only a small radioisotope producing accelerator facility and hence lower investments compared to a reactor. Therefore, the number of cyclotrons is expected to grow even further.

Radioisotopes are frequently traded across borders, especially those produced in reactors. The High Flux Reactor in Petten (the Netherlands) and the BR2 Reactor in Mol (Belgium) are the largest production facilities in Europe. These reactors produce 90% of all radio-isotopes used for medical applications in Europe with respectively a share of 60% for HFR and 30% for BR2.(IRE, personal communication)

With respect to the use of radioisotopes for diagnostic purposes, which are about 90% of the total number of procedures with radioisotopes, ^{99}Mo is used in more than 70% of all nuclear medicine diagnostics. 85% of the production of ^{99}Mo worldwide is done on 5 reactors: the Nuclear Research Universal reactor in Canada (35%), the High Flux Reactor in Petten, the Netherlands (25%), the Safari reactor in South Africa (10%), the BR-2 reactor in Mol, Belgium (10%) and the OSIRIS Reactor in Saclay, France (5%).(IRE, personal communication)

4.2.2 Organisation of radioisotope production in Belgium

Belgium is an important player on the market of radioisotopes for medical applications, through the National Institute of Radio-elements (IRE: Nationaal Instituut voor Radio-elementen/Institut National des Radioéléments). The Institute manages the production of medical radioisotopes. It prepares the targets, sends them to reactors they are working with (BR2, HFR and OSIRIS Reactors) to irradiate and finally prepares radioisotopes for sale to companies who prepare the radiopharmaceuticals. More than 95% of the isotopes produced by IRE are exported throughout the world. IRE is a public utility company, operating as a private organisation but with a board appointed by the Belgian federal government (http://www.entreprises-wallonnes.com/ire-fleurus/profil_en.html). IRE is located in Fleurus, where the processing of ^{99}Mo and other radioisotopes is centralised.

In addition to the production of medical radioisotopes (besides ^{99}MO, IRE also produces ^{131}I, ^{133}Xe, ^{188}Re and ^{90}Y), the IRE also manages control networks for monitoring of air and water radioactivity, manages radioactive waste, engineers and maintains nuclear installations, performs (through its subsidiary Transrad S.A.) logistics and transport of radioactive and fissile material and provides public information and education to professionals. The IRE performs radiological monitoring for the Federal Agency of Nuclear Control, as is the Belgian Nuclear Research Centre (SCK/CEN), the Scientific Institute for Public Health (WIV/ISP) and the University Faculty of Agronomic Sciences of Gembloux. Concerning the monitoring of the environment, IRE has installed automated radiological control probes in France, the Netherlands, Morocco and Belgium.

Key points

- **In terms of production volume, therapeutic radioisotopes are accountable for about 9.5% of the world market. 85.5% of the production of radioisotopes is for diagnostic use.**
- **Due to the relatively higher prices of therapeutic radiopharmaceuticals, the turnover (trade volume in monetary terms) of these radioisotopes is higher, about 20%.**
- **Belgium has a relatively high number of accelerators to produce radioisotopes, compared to other countries.**
- **The Belgian Institute of Radio-elements (IRE) plays a leading role in the production of radioisotopes worldwide.**

4.3 CONSUMPTION OF RADIOISOTOPES

Data on the volumes of consumption of radioisotopes, either for therapeutic or for diagnostic use, are hard to find. Several international organisations (the Joint Research Centre of the European Commission, the International Atomic Energy Association, United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR)) have tried to collect information on either volumes or prices or both but none of the surveys were very successful. The researchers who performed the surveys revealed that at the governmental level, information was usually not available. Therefore they had to rely mostly on the –often incomplete- information from professional societies of nuclear medicine or individual centres for nuclear medicine.

For the comparison of volumes of radiopharmaceuticals used for therapeutic purposes, this report relies on the information of 2002 provided by the report of JRC[1] and was supplemented with more recent information from national reports. For the comparison of volumes of radiopharmaceuticals used for diagnostic purposes, information was collected through an extensive search for country reports of organisations for nuclear medicine or agencies for radio-protection, relevant web-sites of national and international organisations and through personal contacts.

The most recent international comparative data on radioisotopes used for medical purposes were published in 2000 by the UNSCEAR and related to data of 1991-1996. Because of the rapidly moving field of nuclear medicine, these data are probably less relevant for the current situation. In 2008, the UNSCEAR will publish a new report on medical radiation exposures with data of 1995-2002 which will contain –amongst other things- more information on the use of medical radioisotopes in different countries throughout the world. Preliminary insight by the KCE into the data was not granted by the UNSCEAR.

4.3.1 All nuclear medicine services

In general a positive relationship exists between availability of equipment and frequency of procedures. Hence, the more gamma cameras are available in a country, the higher the number of diagnostic nuclear medicine procedures is likely to be. For treatment, this relationship is probably less important, as the number of therapy centres will not dramatically increase the number of patients treated with radionuclides.

Table 20 presents the number of nuclear medicine services and the number of gamma cameras in five countries. For countries with a private and public health care sector (UK, Italy, France), the figures present the total number in both sectors.

Table 20: Number of gamma cameras and nuclear medicine services (private + public) in 2003 (unless mentioned otherwise)

Country	Number of gamma cameras	Number of nuclear medicine services	Number of specialists nuclear medicine
Belgium			318° (224 accredited)
France***	404 (in 2005)	248 (in 2007)	445 (Medical Council) (375 accredited)
UK (Hart and Wall)	384	252	
Italy	300 (in 2004)	253	
The Netherlands		66 (in 2006) *	98 **

* Source: Meeuwsen, personnal communication
** Source: Giesbers H (red.)[4]
*** source: Société Française de Médecine Nucléaire et Imagerie Moléculaire (http://www.sfbmn.org/)
° Source: Annual report 2006 of the National Institute for Health and Disability Insurance.[5]

Most countries do not systematically collect data on the medical use of radioisotopes. Such data are occasionally collected in the context of individual research projects. Relevant data were found for the UK and the Netherlands in two study reports.[6, 7]. The UK report presents data for all nuclear medicine procedures together but provides details for separate sub-sectors in appendix; the Dutch report is split into a part on diagnostic applications and a part on therapeutic applications. We first briefly discuss the general results of the UK report for the entire sector and then separate out the diagnostic and therapeutic applications from both reports (paragraphs 1.3.2. and 1.3.3.). We tried to collect similar information for Belgium, but the professionals told us that they could impossibly provide such data.

Hart and Wall (2005) collected data on the frequency of use of radioisotopes in the UK between April 2003 and April 2004.[7] The authors performed a survey in 240 NHS sites performing nuclear medicine procedures. The response rate to the survey was 66%. To obtain estimates for the frequency of nuclear medicine procedures for the entire UK NHS, the authors extrapolated the findings from the responders to the non-responders, by using the observed correlation between the number of procedures and number of gamma cameras at a site.[7]

The annual number of nuclear medicine procedures was about 11 per 1 000 inhabitants in 2003/2004 in the UK NHS. This meant an increase of 38% compared to 1993/1994. Especially the volume of imaging procedures has increased dramatically: 90% over the last 20 years. Over the last two decades, the number of non-imaging procedures (e.g. measurement of glomerular filtration rate for the kidneys using EDTA) and therapeutic procedures has remained fairly stable. Table 21 shows the absolute number of administrations and the number per 1 000 population (based on a population of 60 million people) for the top 20 nuclear medicine procedures in the UK between April 2003 and March 2004.

Table 21: Top 20 nuclear medicine procedures in the UK NHS (2003/2004)

Procedure	Radionuclide	Chemical form	Number of administrations	
			Absolute number	Number per 1 000 population
Bone scan (planar 98%, SPECT 2%)	^{99m}Tc	Phosphates	197 000	3,28
Lung perfusion (planar 99.99%, SPECT 0.01%)	^{99m}Tc	MAA	95 000	1,58
Myocardium (SPECT 98%, planar 2%)	^{99m}Tc	Tetrofosmin	63 000	1,05
Lung ventilation	^{81m}Kr	Gas	41 000	0,68
Kidney	^{99m}Tc	MAG3	30 000	0,50
Kidney	^{99m}Tc	DMSA	29 000	0,48
Glomerular Filtration Rate measurement	^{51}Cr	EDTA	23 000	0,38
Myocardium (SPECT 87%, planar 13%)	^{99m}Tc	Sestamibi	23 000	0,38
Lung ventilation	^{99m}Tc	DTPA	16 000	0,27
Myocardium (SPECT 98%, planar 2%)	^{201}Tl	Thallous chloride	16 000	0,27
Lung ventilation	^{99m}Tc	Technegas	14 000	0,23
Thyroid	^{99m}Tc	Pertechnetate	11 000	0,18
Thyrotoxicosis therapy	^{131}I	Iodide	10 000	0,17
Cardiac blood pool	^{99m}Tc	Normal erythrocytes	10 000	0,17
Tumours (PET)	^{18}F	FDG	9 000	0,15
Infection, inflammation, tumours	^{99m}Tc	Exametazime	8 000	0,13
Helicobacter Pylori Test	^{14}C	Urea	7 000	0,12
Kidney	^{99m}Tc	DTPA	6 000	0,10
Lung ventilation	^{133}Xe	Gas	6 000	0,10
Cerebral blood flow (SPECT 94%, planar 6%)	^{99m}Tc	Exametazime	5 000	0,08

Source: Hart D and Wall BF, 2005, A survey of Nuclear Medicine in the UK in 2003/2004. Health Protection Agency; Chilton, UK.[7]

When grouped by organ or system under investigation, procedures related to the bones are performed relatively most frequently, followed by procedures related to the lungs and the cardiovascular system.

Table 22: Relative frequency of procedures grouped by organ or system under investigation

Organ or system	% of total number of administrations
Bone	29.6
Lung	25.6
Cardiovascular	16.9
Kidney, urinary system, adrenals	13.8
Thyroid/parathyroid	5.1
Infection, inflammation, tumours	3.8
GI tract	2.1
Brain	1.0
Haematology	0.6
Metabolism	0.6
Liver, spleen, pancreas	0.5
Other	0.4
Total	100

Source: Hart D and Wall BF, 2005, A survey of Nuclear Medicine in the UK in 2003/2004. Health Protection Agency; Chilton, UK.[7]

4.3.2 Diagnostic applications

The *Informatiesysteem Medische Stralingstoepassingen* has published a report on nuclear medicine in the Netherlands in 2007, using data of 2005.[6] About 350 000 diagnostic nuclear medicine procedures have been performed in 2005 in the Netherlands. As in most countries, the volume of nuclear medicine procedures has increased rapidly in the last decade. An increase in the number of nuclear diagnostic procedures of 75% has been observed between 1991 and 2005.

The most frequent nuclear diagnostic procedures in the Netherlands were cardiovascular imaging procedures and bone scans and lung perfusion imaging procedures. In the UK, the by far most frequent diagnostic nuclear imaging procedure was bone scans, followed by lung perfusion imaging and myocardium imaging (Table 23).

Table 23: Volume of nuclear medicine procedures

	UK (2003/2004)		The Netherlands (2005)	
	Absolute numbers	**Per 1 000 people**	**Absolute numbers**	**Per 1 000 people**
Cardiovascular	115 404	1.92	104 300	6.397
Bone	201 087	3.35	101 800	6.243
PET examinations	12 116	0.20	22 500	1.4
Endocrinology (adrenals, lymph system, parathyroid, tyroid)	22 572	0.38	38 000	2.33
Brain	7 205	0.12	2 400	0.147
GI tract, Liver and spleen	7 576	0.12	4 500	0.276
Urinary system + kidney	65 477	1.085	11 300	0.693
Lung	172 723	2.88	37 600	2.306
Infection/Inflammation/tumours	14 389	0.24	3 500	0.215
Other	1 622	0.03	22 200	1.362

Sources:
The Netherlands: Meeuwsen EJ, 2007.[6]
UK: Hart D and Wall BF, 2005.[7]

For some procedures, the nuclear physician has a choice between different radiopharmaceuticals. Table 24 presents the relative use of radioisotopes in cases where different radioisotopes can be used for the same test in the general hospitals in the Netherlands and in the UK NHS.

Table 24: Percentage of different radionuclides used for the procedure in the UK and in general hospitals in the Netherlands.

	Radionuclide	UK	The Netherlands
Thyroid uptake	^{131}I	15.3 %	56.5 %
	^{99m}Tc	49.2 %	
	^{123}I	35.5 %	43.5 %
Thyroid	^{99m}Tc	81.4 %	20 %
	^{123}I	5.0 %	79 %
	^{131}I	13.6 %	1 %
Lung ventilation	^{99m}Tc	40.0 %	2 %
	^{127}Xe or ^{133}Xe	7.2 %	16 %
	^{81m}Kr	52.7 %	82 %
Myocardium	^{201}Tl	15.5 %	30.72 %
	^{99m}Tc	84.5 %	69.28 %
	^{111}In	0 %	0 %
Myocardium redistribution	^{201}Tl	N.A.	100 %
	^{99m}Tc	N.A.	0 %
Myocardium Effort	^{99m}Tc	N.A.	88 %
	^{201}Tl	N.A.	12 %
Myocardium rest	^{99m}Tc	N.A.	72 %
	^{201}Tl	N.A.	28 %
Leucocytes	^{99m}Tc	N.A.	18 %
	^{111}In	N.A.	82 %

N.A.: not available, meaning that these data were not separately available for the country.
Source: Meeuwsen EJ, 2007.[6]

Quite important differences exist in the relative use of different radioisotopes for the same examination between the countries. For thyroid uptake imaging, the general hospitals in the Netherlands apply ^{131}I in the majority of cases (56%), while this radioisotope is used in only 15% of the cases in the UK. Similarly, for thyroid imaging, the UK tends to prefer ^{99}Tc^{m} (81%) while the Netherlands uses ^{123}I relatively most frequently (79%).

4.3.3 Therapeutic applications

In the UK, about 14 000 administrations of radioisotopes were reported for therapeutic procedures. In the Netherlands, the number of therapies with radiopharmaceuticals *in general hospitals* is estimated at 3 500 in 2005.[6] No data were available for the academic hospitals. In 2001, academic hospitals performed about 3 000 therapies with radioisotopes. More recent data have not been collected.

In both the UK and the Netherlands the most frequent therapeutic procedure is ^{131}I treatment for hyperthyroidism (Table 25). This treatment makes up 75% of all therapeutic procedures with radiopharmaceuticals.[6, 7] Other frequent nuclear medicine therapies are treatment of thyroid carcinoma, treatment of bone metastases with ^{89}Sr and treatment of arthritic conditions. The relative number of treatments of non-toxic goiter with radiopharmaceuticals is low in the UK compared to the Netherlands due to the fact that most hospitals that responded to the UK survey did not keep separate statistics on this condition but classified it under thyrotoxicosis.

However, it is thought that this misclassification accounts for less than 1% of the number of treatments for thyroxicosis.

Table 25: Number of procedures and relative share in total number of procedures for therapeutic applications of radioisotopes

	UK	Netherlands (general hospitals only)
Thyroid disease		
Carcinoma	1692 (12.1%) (^{131}I)	336 (9.6%)
Thyrotoxicosis	10 423 (74.6%) (^{131}I)	2 625 (75%)
Non-toxic goiter	261 (1.9%) (^{131}I)	140 (4%)
Malignant disease	156 (1.1%) (^{131}I)	
Polycythaemia vera	184 (1.3%) (^{32}P)	
Bone metastases ^{153}Sm ^{89}Sr ^{186}Re	 94 (0.7%) 480 (3.4%) 7 (0.05%)	 28 (0.8%) 154 (4.4%) 84 (2.4%)
Arthritic conditions	330 (2.4%) (^{90}Y)	126 (3.6%)
Thrombocythaemia	1 (0.01%) (^{32}P)	42 (1.2%)
Thyroid ablation	114 (0.8%) (^{131}I)	
Antibody therapy	75 (0.5%) (^{131}I)	
Hepatic tumour	9 (0.06%) (^{131}I)	
Lymphoma, Anti-B1	13 (0.09%) (^{90}Y)	
Liver cancer	7 (0.05%) (^{90}Y)	
Carcinoid	86 (0.6%) (^{90}Y)	
Neuroblastoma	39 (0.3%) (^{90}Y)	

Key points

- **Most frequent nuclear medicine procedures in the UK are bone scans, lung perfusion and myocardium scans**
- **There is a lot of variation between countries in the relative use of radioisotopes in cases where there is choice between different radioisotopes for one procedure.**
- **The most frequent therapeutic procedure with radionuclides is thyroid disease therapy.**

4.4 FINANCING OF RADIOISOTOPES

4.4.1 The Netherlands

4.4.1.1 General reimbursement principles

Since February 2005, the Netherlands has introduced a health care reimbursement system for hospitals and medical specialists based on diagnosis treatment combinations (DBCs: diagnose-behandeling combinaties). A DBC defines the set of activities and interventions provided in hospitals to patients with a specific diagnosis. It covers the entire health care path in hospital, including all hospital activities and time and effort of medical specialists.[8]

DBCs either have a fixed (list A) or negotiable (list B) reimbursement price. List A DBCs cover about 90% of all hospital costs, list B 10%.[8]

The price of a DBC consists of a hospital cost component and an honorarium for medical specialists. For list A, the hospital cost component has been determined on the basis of resource use and unit cost data from approximately 20 hospitals. The honorarium component was determined on the basis of time and motion studies. The fee per hour of specialist time was set at €140. For list B, the hospital cost component of the DBC prices are negotiated between hospitals and health insurers. The honorarium component remains fixed.[9]

In both lists, the hospital cost component in the DBC price covers wages, medication, medical materials, housing and equipment and overheads. In list B also the costs of capital should be covered by the hospital cost component.[9]

4.4.1.2 Reimbursement of radioisotopes

The reimbursement of radioisotopes for diagnostic or therapeutic purposes is integrated in the DBCs for medical imaging, both for inpatient and out-patient services.

The share of the radioisotopes costs in the tariff of the relevant DBCs is not publicly available. The 20 pioneering hospitals were only obliged to provide information about unit costs of intermediate products and not about the different cost components. Intermediate products are for instance hospital days, day-care days, outpatient visits, laboratory tests or diagnostic interventions. Cost components of these intermediate products are for instance the volume and unit cost of radioisotopes used for a medical imaging procedure. At the central governmental level, hence, no information on unit costs or volumes of use of radioisotopes is available.

Different ways of allocating costs of radioisotopes to intermediate products are applied, depending on the information available. No rules are imposed for the allocation the costs to intermediate products, but the general principle is to pursue as much as possible a direct allocation. If the costs of different isotopes are booked on one account, data on unit prices and quantities of radioisotopes used for a procedure are used to allocate the costs to a procedure. If separate accounts are held for separate isotopes, the total amount spent on the isotope is divided by the number of procedures that uses the isotope to obtain a radioisotope cost per procedure. (Personal communication Niek Bossché, Erasmus MC Rotterdam)

Radioisotopes for therapeutic use

Tariffs for a number of treatments with radioisotopes are presented in table 26. The tariff consists of a hospital cost component and an honorarium for the physician. The hospital cost component covers the consumables (including the radiopharmaceuticals) and the operating costs. These are tariffs for so-called supporting services.

Brachytherapy, including treatment of prostate cancer with ^{125}I but also other types of brachytherapy, is reimbursed through a DBC tariff on list A. Separate codes and hence separate tariffs exist for different types of brachytherapy. A classification is made according to the organ. The DBC-code for brachytherapy for urological tumours is 140634. The tariff includes a hospital cost component of €13 806, a honorarium of €1 823.30 and a hospital-specific supplement (which can be up to 100% of the hospital cost component). The hospital cost component is supposed to cover the cost of the radioisotope. There is no specific tariff for the acquisition of seeds but a Maastricht hospital indicated us that a mean of 80 seeds at 0.45 mCi/seed is ordinarily implanted for a total cost of 3 400 EUR + VAT (42.50 EUR/seed).

Table 26: DBC tariffs for treatments with radioisotopes

Code supporting service	Tariff			Description
	Total	Hospital cost component	Honorarium	
120400	368.00	235.00	133.00	Treatment of hyperthyroidism with ^{131}I
120401	368.00	235.00	133.00	Treatment of large goiter with ^{131}I
120402	544.50	411.50	133.00	Treatment of thyroid neoplasms with ^{131}I (401)
120403	309.50	176.50	133.00	Treatment with radioactive colloid per weight
120404	544.50	411.50	133.00	Treatment of pleura-exudate/ascites with radioactive colloid
120405	485.00	352.00	133.00	Treatment of polycythemia vera with ^{32}P (402)
120406	2,482.00	2349.00	133.00	Treatment of painful bone metastasis with ^{89}Sr (405)
120407	1,014.00	881.00	133.00	Treatment of painful bone metastasis with ^{186}Re (406)
120408	1,014.00	881.00	133.00	Treatment of painful bone metastasis with ^{153}Sm
120410	2,482.00	2 349.00	133.00	Treatment of neuro-endocrine tumours (MIBG-High) (407).

Radioisotopes for diagnostic use

Diagnostic procedures with radioisotopes are intermediate products. They are included in the DBC tariffs. A list of tariffs is presented in appendix. It is noteworthy that DBCs related to nuclear medicine are on some occasions restricted. For instance, the DBC for SPECT of lungperfusion cannot be combined with a DBC for SPECT of lungventilation with perfusion.

4.4.2 France

4.4.2.1 General reimbursement principles

The French health care reimbursement system is currently in transition. It is moving from a system that is mainly based on global budgets for public or private not-for-profit hospitals and on per diem rates and fee-for-service for private for-profit hospitals towards a case-mix-based reimbursement system for all hospitals. In France, this per-case payment system is called "Tarification à l'activité" (T2A). Per-case payment will be based on the definition of GHMs ("Groupes Homogènes de Malades"). GHMs are a variant of the US DRG-classification.[10]

The private for-profit sector has already entirely moved to a case-mix based system for all activities in the medical, surgical and obstetric wards (since March 1st, 2005). The public and not-for-profit private sector is still in transition. The part of the medical, surgical and obstetric activities paid for by the case-mix system is increasing gradually each year but complete transition in the entire hospital sector is expected for 2012. Until then, activities not paid for by the case-mix system in the public hospitals are being funded by global budgets. During the transition period, "national prices" can still be adjusted to the providers' historical costs. This applies to both the private and the public sector.[10]

In the per-case payment system, in-patient acute care will be financed through a payment per case, based on a classification system for homogeneous stays (GHS: Groupes homogènes de séjours). The GHS payment covers nursing care, accommodation and infrastructure for hospitalised patients, day-case treatments, hospital drugs and capital investment costs. For public and private not-for-profit hospitals, the GHS payment also covers medical and technical acts by doctors (but not consultations). The prices of the GHS are determined on the basis of average cost data per GHM of, at present, 52 public and private not-for-profit hospitals.

For private for-profit hospitals, medical and technical acts (and consultations) are paid for separately on a fee-for-service basis (according to the NGAP (Nomenclature Générale des Actes Professionels) and CCAM (Classification Commune des Actes Médicaux). These systems are conceptually comparable to the Belgian nomenclature. The CCAM is supposed to replace the NGAP during the transition to the per-case payment system, but it is unclear when the replacement will actually take place. Currently, both lists co-exist. The CCAM applies to procedures performed by physicians and dentists; the NGAP applies to physician's visits and consultations and to procedures performed by other health professionals in private practices (nurses, physiotherapists, speech-therapists and orthopaedists).

Out-patient care, including medical procedures such as medical imaging, lab tests and consultations, will be paid on a fee-for-service basis (CCAM). The CCAM and NGAP fees cover the production costs of each procedure and the honorarium of the physician.

Expensive drugs or medical devices will be paid separately on a real cost basis. These drugs and devices have to be defined by the National Union of Health Insurance Funds (UNCAM: "Union Nationale des Caisses d'Assurance Maladie") and the price declared by the laboratory or, if this price is questioned, to the price fixed and published by the Committee for Medical Products (CEPS: "Comité Economique des Produits de Santé")

4.4.2.2 Reimbursement of radioisotopes

Radioisotopes for therapeutic use

In the CCAM a tariff is fixed for therapies with radioisotopes. For prostate brachytherapy with ^{125}I, the CCAM tariff for the application of the radioactive seeds by the urologist is €334 (CCAM JGNL001), but this does not include the cost of ^{125}I. Like drugs, ^{125}I is reimbursed on top of the CCAM tariff.

Brachytherapy as monotherapy is exclusively reimbursed for patients with a local prostate cancer where the following conditions are met:

- Intraprostatic localisation, maximal grade T2a (extension limited to one lobe);
- PSA level lower than 10 ng/ml;
- Small volume of the tumor;
- Well differentiated cancer (Gleason score lower than 7);
- Volume of the prostate lower than 50 cm^3 ;
- Absence of avert mictional troubles which could decompensate after the application.

The treatment with permanent seeds is only reimbursed in the centres where a specialised room is available and the collaboration between urologists, radiotherapists and dosimetry physicists is guaranteed. All these specialists must have followed both theoretical lessons and a specific training in an expert centre.

The reimbursement tariffs for the ^{125}I seeds are presented in table 27. ^{125}I is fully reimbursed, patients do not pay a co-payment.

The tariffs are at the same time maximum tariffs that have been negotiated with the providers for a specific period of time. After this period, prices have to be re-negotiated. The reimbursement of the seeds is limited up to a maximum number of 90 seeds at €44.12 per seed or €3970.80 (LPP 3407481, 3407765, 3419461, 3429643, 3429979, 3441845, 3442299, 3454463, 3469720, 3495870).

Table 27: Reimbursement tariffs for ^{125}I in France

Code	Reference	Company	Intervention	Maximal public price
3469720	Grain iode 125, Amersham, ONCOSEED/ECHOSEED, cartouche de 15 grains.	Amersham Health SAS	€661.80 till 02-02-2010	€661.80
3454463	Grain iode 125, Amersham, RAPID STRAND, 10 grains.	Amersham Health SAS	€441.20 till 02-02-2010	€441.20
3441845	Grain iode 125, Eckert & Ziegler Bebig GmbH, Isoseed I-125, le grain.	Eckert & Ziegler Bebig GmbH (Bebig GmbH)	€44.12 till 02-02-2010	€44.12
3429643	Grain iode 125, Bebig GmbH, Isocord I-125, chaîne grain lié, le grain. Chaîne de grains d'iode liés Isocord I-125 pouvant contenir jusqu'à 75 grains maximum.	Eckert & Ziegler Bebig GmbH (Bebig GmbH)	€44.12 till 02-02-2010	€44.12
3419461	Grain iode 125, Bard, BRACHYSOURCE PS-1251LCE, le grain.	Bard France SAS (Bard)	€44.12 till 30-09-2011	€44.12
3495870	Grain iode 125, Bard, BRACHYSOURCE PS-1251CCE, cartouche, le grain. Cartouche pouvant contenir jusqu'à 15 grains libres maximum.	Bard France SAS (Bard)	€44.12 till 30-09-2011	€44.12
3429979	Grain iode 125, IBT, INTERSOURCE, grain isolé, le grain, réf DRN 5350	International Brachytherapy SA (IBT)	€44.12 till 30-03-2012	€44.12
3442299	Grain iode 125, IBT, INTERSOURCE, cartouche, le grain libre, réf DRN 5351 B Cartouche contenant 15 grains libres maximum.	International Brachytherapy SA (IBT)	€44.12 till 30-03-2012	€44.12
3407765	Grain iode 125, IBT, INTERSTRAND, grain lié, le grain, réf DRN 5352	International Brachytherapy SA (IBT)	€44.12 till 30-03-2012	€44.12
3407481	Grain iode 125, Nucletron, SELECTSEEDS, cartouche, le grain Cartouche contenant de 50 à 100 grains libres maximum.	Nucletron France (Nucletron)	€44.12 till 30-03-2012	€44.12

Maximal coverage of **€3 970,80** per patient, all taxes inclusive.

Some radiopharmaceuticals for therapeutic use are figuring on the list of expensive drugs: Metastron, ^{89}Sr, ^{90}Y (Ytracis). (http://agmed.sante.gouv.fr/htm/3/t2a/html/indt2a.htm) Zevalin, used for the preparation of an injectable radiopharmaceutical, is also figuring on this list. These products are limited to hospital use. Their reimbursement occurs separately on top of the GHS at the real cost or at a maximum price determined by the CEPS. For Zevalin, the maximum price is set at €11 128.9 (VAT incl.), for Metastron at €1 324.24 and for Ytracis at €2 042.

To figure on the list of expensive drugs (or devices), three conditions have to be fullfilled:

- the cost of the drug (or implant) is particularly high
- the products in question introduce heterogeneity within the GHM costs and GHS tariffs

- the drugs (and implants) have to be included on a list established by ministerial order and/or by the National Union of Health Insurance Funds (UNCAM) every year.

Hospitals using expensive drugs or implants on the list have to sign contracts with the Regional Hospital Agencies (ARH: "Agences Régionales de l'Hospitalisation") on The fee ranges from €550 to €1000, depending on whether it concerns a PET only or PET-CT and depending on the yearly number of scans. the proper use of these products. 'Proper use' is defined in this context as use according to nationally and internationally accepted medical standards. Hospitals not complying with these standards get lower reimbursement rates.

Radioisotopes for diagnostic use

In public hospitals, the GHS tariff covers all expenses. In private hospitals, the GHS tariff does not include practitioners' fees which are reimbursed using the NGAP/CCAM tariffs. For PET, a special tariff is used which covers the fees for the radiologist, the use of equipment and the radiopharmaceutical. Above a certain threshold activity (>1000 acts), the tariff decreases.

The special tariff applies to private hospitals and private radiological structures or to outpatients in public hospitals. For inpatient care in public hospitals, the GHS covers all costs. An exception exists for products figuring on the list of very new products. These may be bought by the hospital pharmacy on a special innovation fund.

4.4.3 USA

The treatment of interstitial brachytherapy with Low Dose Rate ^{125}I is reimbursed as "complex interstitial radiation source application" under the APC code 651 at $661.21 (CPT code 77778).

4.4.4 Italy

4.4.4.1 General reimbursement principles

The Italian health care financing system is characterised by a high level of decentralisation. The regions have the responsibility to provide so-called essential levels of care (LEAs: *Livelli Essenziali di Assistenza*), defined by the central government, to their residents. After a negotiation process, regions receive funds (capitation payments) from the central government to finance the provision of healthcare services. If these funds are insufficient to pay for all the services defined by the LEAs, regions should use local taxes to guarantee provision of the essential services. Alternatively, the regions may also decide to provide additional services to their citizens, for instance if they achieve efficiency gains or if they are prepared to put their own resources in additional healthcare services.

Since 1995, inpatient care (both hospitalisation and day-care) is being financed by means of a DRG-based system. The list of DRGs is defined at the central level, but the regions have the autonomy to define the tariffs. All types of services provided during hospitalisation are supposed to be fully reimbursed by the regions, *if* delivered appropriately. As the list of DRGs also includes diagnoses for which hospitalisation is not necessarily appropriate, not all DRGs are reimbursed.

Specialised out-patient (ambulatory) care, including visits, diagnostic and curative activities covered by the Italian NHS is defined in a positive list. This list also defines the tariffs used for reimbursement of providers (fee-for-service). Regions are free to define their own reimbursement rates within limits (the national reimbursement rates are maxima), but are not allowed to modify the list of reimbursable services. In addition, a negative list exists, defining the specialised out-patient care not covered by the Italian NHS. The services on the positive list are classified according to the organ the intervention relates to.

Some services on the list are limited to specific settings, e.g. with specific equipment. For some services, reimbursement is conditional upon the clinical condition of the patient. This applies for instance to diagnostic exams that are very costly, such as PET-scans.

Diagnostic imaging and nuclear medicine procedures are included in the essential levels of care (LEAs). Hence, these services are completely funded by the regions for all citizens.

4.4.4.2 Reimbursement of radioisotopes

As all regions are actually free to define their reimbursement tariffs -be it within the national reference limits- it is impossible to determine the implicit reimbursement level of radioisotopes. In general, the costs of radiopharmaceuticals are included in the regional tariffs but in some cases the tariff does not cover the costs of the tracer (personal communication Lorenzo S. Maffioli). The radiopharmaceuticals can be purchased abroad, produced in a centre's own cyclotron or bought from another centre that has a cyclotron.

For specialised out-patient services, such as radiotherapy and nuclear diagnostic procedures, fees were negotiated at a central level but the regions kept autonomy to adapt the negotiated fees.

It is unclear whether at the start of the negotiations any cost assessments were made. In 1997, the Lombardy region established a special committee for "cost analysis and updating of tariffs for out-patient specialist services". The cost analysis was based on the data from different institutions that provided out-patient specialist care or diagnostic services. Eventually, the adaptation of the national tariffs in Lombardy was not based on the cost assessment alone. Other criteria, such as the expected financial impact on regional and patient out-of-pocket expenses, existence of waiting lists, availability of technology were also taken into account.

Radioisotopes for therapeutic use

Treatments with radioisotopes are listed in the DRG system for hospital care or the fee schedule for ambulatory care. The radioisotope used for the procedure is not specified. The tariffs differ by region, but the *Associazione Italiana di Medicina Nucleare ed Imaging Molecolare* (AIMN) presents estimated average reimbursement tariffs for Italy on its web-site (www.aimn.it). The procedures and estimated national average tariffs are listed in table 28.

Table 283: Estimated national average reimbursement tariffs for treatment with radioisotopes in Italy (2007)

Injection or instillation of radioisotopes (intracavitary, intravenously)	Estimated national average tariff
Treatment of hyperthyroidism (up to 370 MBq)	€ 67,60
Treatment of hyperthyroidism (from 370 MBq onwards)	€ 14,20
Endocavitary treatment	€ 179,99
Treatment with monoclonal antibodies (up to 185 MBq)	€ 526,79
Treatment with monoclonal antibodies (from 185 MBq onwards)	€ 219,49
Palliative treatment of painful bone metastasis	€ 826,33

Radioisotopes for diagnostic use

The costs of radioisotopes are included in the tariffs of the regional fee-for-service schedule. The estimated average reimbursement tariffs for Italy are presented in appendix 2.

4.4.5 United Kingdom

4.4.5.1 General reimbursement principles

The basic principle of the National Health Service (NHS) is that everyone has a right to free health care, based on clinical need, appropriateness and cost-effectiveness. However, the health care benefit package does not include specific entitlements to services; neither does it explicitly exclude many services. Exceptions exist in the domains of medicines and screening, where exclusions are explicitly stated. Thus, all services are defined implicitly, in the sense that there are no positive lists of treatments to which patients are entitled. Patients' entitlements are therefore inferred from, for instance, national guidelines from the National Service Frameworks (NSF), decisions by the National Institute of Clinical Excellence (NICE), existence of co-payments and complementary funding by the NHS. NICE and NSF may prove to have an important role in the future development of a positive list of benefits and entitlements.[11]

The UK health care financing system relies on tax revenues. Each year, the Parliament allocates a proportion of the total revenues to the NHS for the provision of health care. Primary Care Trusts (PCTs) are responsible for about 82% of the flow of the NHS funding. PCTs purchase primary care and hospital services and may also run community hospitals and employ community nurses. The allocation of the overall budget for the PCTs to the individual PCTs occurs through a capitation payment formula, taking into account population characteristics, and unavoidable differences in the costs of resources.

Major players in the hospital sector (inpatient and outpatient care) are NHS trusts. The UK hospital financing system is now moving from a system based on block or cost-volume contracts between purchasers (PCTs) and providers (NHS Trusts) to a system based on "Payment by Results" (PbR). The former contracts –or service level agreements- were not binding but intended to enable parties to agree on matters of quality, quantity and price.

"Payment by Results" is a case payment system, similar to DRG payment systems. The tariffs for procedures are set at national level. Tariffs are classified by Health care Resource Group (HRG), defined by diagnosis and complexity, and are based on the average costs for that procedure (i.e. the reference cost) of all NHS hospitals. For the calculation of the HRG tariffs each condition or procedure is defined in terms of its resource profile. This involves identifying the main cost drivers for each procedure (e.g. drugs used, bed days, time spent in the operating theatre,…), defining unit costs of each cost driver and finally multiplying quantities of cost drivers with unit costs, very alike the Dutch DBC system.

The HRG tariffs cover an entire period of hospitalisation, from admission to discharge of the individual patient. They apply to inpatient care and day-care. Geographical adjustments are made to the tariffs to take account of the unavoidable area-specific costs. The aim is to adjust the tariffs every year to respond to trends in average costs, increases in efficiency, new technology, investments in quality and other reforms and technical changes in NHS funding or accounting practice. Tariffs are still evolving and are not yet fully formed. Currently, the tariffs cover only elective care (about 550 HRGs) and are mandatory for NHS trusts. This is about 30% of the current value of hospital activities. The aim is to include non-elective and outpatient PCTs continue to negotiate contracts with providers. This means that prices for activities that are not covered by the PbR system can be locally negotiated and hence differ for each purchaser.

For specific diagnostic and treatment services (e.g. orthopaedics) the Department of Health has procured contracts with independent (private) providers. The reason for these contracts was that capacity within the NHS was deemed insufficient to guarantee adequate access to appropriate care. The prices negotiated in these contracts are generally higher than the PbR tariffs. PCTs have to use the independent service facilities following the tariffs negotiated by the Department of Health. In addition they can also contract directly with the private sector themselves for these services.

4.4.5.2 Reimbursement of radioisotopes

Radioisotopes for therapeutic use

Radiotherapy is currently not yet included in the PbR financing system, pending on the introduction of the new HRG tariffs in 2009. Funding depends therefore on local negotiation between commissioners and providers. Typically, but not necessarily, this is by means of a block contract. In the private sector in the UK, there already is a private charge for the therapy and a separate charge for the radiopharmaceutical.

Radioisotopes for diagnostic use

In general the costs of radioisotopes for diagnostic use are reimbursed through the relevant inpatient/outpatient tariffs in the PbR financing system. The cost of the radioisotopes is in principle included in the HRG tariff. The Department of Health acknowledges, however, that this is an issue of debate. The inclusion of the cost of the radiopharmaceutical makes the costing procedure for the HRGs difficult. The Department of Health has introduced some indicative tariffs to support unbundling pending on the introduction of new HRG's in 2009/2010.

Nuclear imaging procedures requested by a primary care physician on behalf of the patients are paid for according to negotiated prices between the PCTs and providers. It is expected that these procedures will also be paid for through the PbR system by 2008. In the meantime, data that should allow the calculation of reference costs for these procedures are being collected. Groups of medical imaging procedures are being created according to degree of complexity and cost.

4.4.6 Summary

Table 29 summarises the reimbursement systems for radioisotopes in Belgium, the Netherlands, France, Italy and the UK.

Table 29: Comparison of radioisotope reimbursement system between countries

	Therapeutic radioisotopes		**Diagnostic radioisotopes**	
	Inpatient	Outpatient	Inpatient	Outpatient
Belgium	Reimbursement of invoices for radioisotopes		Fee-for-service (separate fees for the procedure and the isotope used)	
The Netherlands	Included in the DBCs		Included in the DBCs	
France	Reimbursement on top of GHS tariff	Reimbursed on top of CCAM tariff	Included in GHS tariff	Included in CCAM tariff
Italy	Included in DRG payment *some exceptions*	Included in fee-for-service *some exceptions*	Included in DRG payment *some exceptions*	Included in fee-for-service *some exceptions*
UK	Included in HRG tariff		Included in HRG tariff	

Key points

- **For diagnostic use of radioisotopes, most health care systems in our comparison include the cost of radioisotopes in the per-case payment or fee-for-service.**
- **For therapeutic use of radioisotopes, two systems exist: either the cost of the radioisotopes is included in the per-case payment tariff and/or in the fee-for-service (the Netherlands, Italy, UK) or the cost is reimbursed on top of the per-case payment or fee-for-service (France and some procedures in Italy).**

5 APPENDIX

APPENDIX 1: DIAGNOSTIC RADIO-ISOTOPES

^{99m}Technetium

$^{99m}TcO^{4-}$
^{99m}Tc-albumin (^{99m}Tc-HSA) : 21 mg HSA, 0.23 mg $SnCl^2.2H^2O$ under N^2 (Amersham) & 100 mCi ^{99m}Tc; heart blood pool ; 5 mCi; stable for 6 hours.

^{99m}Tc-albumin aggregated (^{99m}Tc-MAA): 2.0 mg human albumin aggregated, 0.5 mg human albumin, 0.12 mg $SnCl^2.2H^2O$, 80 mg lactose, 24 mg succinic acid, 1.4 mg acetate sodium under N^2 (Amersham) & 60 mCi ^{99m}Tc; stable for 6-8 hours.
Perfusion lung imaging (in suspected pulmonary embolism), venography (lower extremity venous thrombosis) and assessment of LeVeen shunt patency; 3-4 mCi

^{99m}Tc-albumin colloid: 0.5 mg human colloidal albumin, 15 mg glucose, 2 mg poliximere 238, 0.5 mg Na_3PO_4, 0.25 mg sodium, 0.2 mg $SnCl^2.2H^2O$, (Nanocoll, Amersham); stable for 6 hours at 2-8°C.
^{99m}Tc-apcitide : 0.1 mg bibapcitide, 75 mg glucoheptonate sodium dihydrate, 0.089 mg $SnCl^2.2H^2O$ under N^2 (AcuTect, Amersham) & 50 mCi ^{99m}Tc; 15 min. in a boiling water bath; stable for 6 hours.
Detection of acute venous thrombosis (lower extremities); 20 mCi

^{99m}Tc-bicisate (^{99m}Tc-ECD) : 0.9 mg bicisate dihydrochloride, 0.36 mg disodium EDTA.$2H^2O$, 24 mg mannitol, 0.072 mg $SnCl^2.2H^2O$ under N^2 (Neurolite) & 100 mCi ^{99m}Tc; stable for 6 hours.
Brain imaging in localization of stroke; 10-30 mCi

^{99m}Tc-depreotide : .050 mg depreotide, 5 mg glucoheptonate sodium dihydrate; 0.10 mg EDTA disodium.$2H^2O$, 0.05 mg $SnCl^2.2H^2O$ under N^2 (NeoTect) & 50 mCi ^{99m}Tc; 10 min. in a boiling water bath; stable for 5 hours.
localization of receptor-bearing pulmonary masses with highly suspected malignancy; 15-20 mCi.

^{99m}Tc-disofenin (^{99m}Tc-DISIDA) : 20 mg disofenin, 0.6 mg $SnCl^2.2H^2O$, under N^2 (Hepatolite, CIS) & 12-100 mCi ^{99m}Tc; stable for 6 hours.
Hepato-biliary agent in diagnosis of acute cholecystitis; 1-5 mCi if bilirubin ≤ 5 mg/ml or 3-8 mCi if bilirubin > 5 mg/ml

^{99m}Tc-exametazime (^{99m}Tc-HMPAO): Ceretec
labeled white blood cells (^{99m}Tc-WBCs):

^{99m}Tc-gluceptate (^{99m}Tc-GH):

^{99m}Tc-mebrofenin (^{99m}Tc-BRIDA): & 100 mCi ^{99m}Tc;
Hepato-biliary agent; 2-5 mCi if bilirubin ≤ 5 mg/ml or 3-10 mCi if bilirubin > 1.5 mg/dL; stable for 18 hours.

^{99m}Tc-medronate (^{99m}Tc-MDP):
bone imaging; 10-20 mCi

^{99m}Tc-mertiatide (^{99m}Tc-MAG3): (TechneScan MAG3, Mallinckrodt) & 100 mCi ^{99m}Tc;
renal imaging; 5-10 mCi; stable for 6 hours.

^{99m}Tc-oxidronate (^{99m}Tc-HDP) : 3.15 mg oxidronate sodium, 0.297 mg $SnCl^2.2H^2O$, 0.94 mg gentisic acid, 30 mg NaCl under N^2 (TechneScan HDP Mallinckrodt) & 300 mCi ^{99m}Tc;
altered osteogenesis ; 10-20 mCi; stable for 8 hours.

^{99m}Tc-Pentetate (^{99m}Tc-DTPA) :
20.6 mg Pentetate-Ca-Na3, 0.30 mg$SnCl^2.2H^2O$ under N^2 (CIS) & 160 mCi ^{99m}Tc;
brain and kidney imaging, cerebrospinal fluid leakage, renal perfusion, glomerular filtration rate, lung ventilation ; 3 mCi in GFR, 5-10 mCi in renal perfusion, 10-20 mCi in brain imaging

^{99m}Tc-pyrophosphate (^{99m}Tc-Ppi) : 11.9 mg pyrophosphate sodium, 4.4 mg $SnCl^2.2H^2O$ under N^2 (TechneScan PYP Mallinckrodt) & 100 mCi ^{99m}Tc;
bone and cardiac infarctus imaging; 15 mCi in these indications; stable for 6 hours.

^{99m}Tc-labeled red blood cells (^{99m}Tc-RBCs): 0.105 mg $SnCl^2.2H^2O$, 3.67 mg citrate sodium. $2H^2O$, 5.5 mg dextrose, 0.11 mg NaCl under vacuum, 3 ml whole blood in ACD or heparin, add 0.6 mg hypochlorite sodium; add 8.7 mg citric acid monohydrate, 32.5 mg citrate sodium dihydrate, 12 mg dextrose anhydrous (Ultratag RBC Mallinckrodt) & 10-100 mCi ^{99m}Tc;
cardiac imaging and gastrointestinal bleeding; 10-20 mCi; stable for hours.

Denatured ^{99m}Tc-labeled red blood cells (^{99m}Tc-RBCs): same as in vitro ^{99m}Tc-labeled red blood cells but extra step of 20 min. at 50°C before injection.
Spleen imaging;

^{99m}Tc-in vivo labeled red blood cells: inject 7.5 mg Sn-Ppi (= half a vial of TechneScan PYP, Mallinckrodt) & 20 min. later inject 20-30 mCi $^{99m}TcO^{4-}$.

^{99m}Tc-modified in vivo labeled red blood cells: inject 7.5 mg Sn-Ppi (= half a vial of TechneScan PYP, Mallinckrodt) & 20 min. later draw 10 ml blood into a syringe containing 20-30 mCi $^{99m}TcO^{4-}$; incubate for 10 min. and then reinject.

^{99m}Tc-sestamibi (^{99m}Tc-6MIBI) : 1 mg tetrakis copper tetrafluoroborate,2.6 mg citrate sodium. $2H^2O$, 1 mg L-cysteine HCl monohydrate, 20 mg mannitol, 0.050 mg $SnCl^2.2H^2O$ under N^2 (Cardiolite, DuPont) & 25-150 mCi ^{99m}Tc; 10 min. in a boiling water bath; stable for 6 hours;
myocardial perfusion; 10-30 mCi

^{99m}Tc-succimer (^{99m}Tc-DMSA) : 1 mg DMSA, 0.70 mg ascorbic acid, 50 mg inositol, 0.420 mg $SnCl^2.2H^2O$ under N^2 & 40 mCi ^{99m}Tc;
kidney imaging; 5 mCi; stable for 4 hours.

^{99m}Tc-sulfur colloid (^{99m}Tc-SC) : 4-step procedure : 2 mg $Na_2S_2O_3$, 2.3 mg EDTA-disodium, 18.1 mg gelatin & 500 mCi ^{99m}Tc; add 1.8 ml 0.148 M HCl; 5 min. in a boiling water bath; add 44.28 mg Na_2HPO_4 & 14.22 mg NaOH in 1.8 ml.
reticulo-endothelial system imaging (1-8 mCi), bone marow imaging (3-12 mCi), lymphoscintigraphy, LeVeen shunts patency, gastroesophageal studies; stable for 6 hours.

^{99m}Tc-tetrofosmin : 0.23 mg tetrofosmin, 0.32 mg sulfosalicylate disodium, 1 mg D-gluconate sodium, 1.8 mg $NaHCO_3$, 0.030 mg $SnCl^2.2H^2O$ under N^2 (Myoview Amersham) & 120 mCi ^{99m}Tc;
myocardial perfusion: 5-8 mCi for stress, then 15-24 mCi at rest; stable for 8 hours.

^{99m}Tc-leukocytes

^{99m}Tc-ethylenedicysteine (^{99m}Tc-EC) :

^{99m}Tc-labelled carbon (Technegas : 7-10 mCi
lung imaging; 1 mCi.

^{99m}Tc-sulesomab (LeukoScan) & 30 mCi ^{99m}Tc; infection and inflammation; mCi ;stable at 4°C for 4 hours.

Expiration time of any ^{99}Mo-^{99m}Tc generator is 14 days after production. At transient equilibrium, the actual ^{99m}Tc activity is 0.946 (=*0.86 x 1.1*) x the ^{99}Mo activity present.

Quality control:

Radioactivity calibration
Chemical purity test for the concentration of aluminium ion (<10 µg Al^{3+} per ml eluate
Radionuclidic purity test for the presence of ^{99}Mo contaminant (< 0.15 µCi ^{99}Mo per mCi ^{99m}Tc)

^{67}Gallium

^{67}Ga-citrate
Hodgkin's disease, lymphoma, inflammatory lesions; 3-8 mCi

^{111}Indium

^{111}In-capromab pendetide (ProstaScint, Cytogen); prostate cancer metastases

^{111}In-ibritumomab tiuxetan (^{111}In-Zvalin); treatment of refratory follicular non-Hodgkin's lymphoma

^{111}In-pentetreotide: 0.010 mg pentetreotide, 2 mg gentisic acid, 4.9 mg citrate trisodium, 0.37 mg citric acid, 10 mg inositol & 3.3 mCi $^{111}InCl_3$ in presence of 22 µM HCl and 4 µg $FeCl_3$ (OctreoScan, Mallinckrodt). neuroendocrine tumors expressing somatostatin receptors; 3-6 mCi; stable for 6 hours.

^{111}In-oxine: 0.050 mg oxine, 0.1 mg polysorbate 80, 6 mg HEPES buffer in 0.75% NaCl solution & 1 mCi $^{111}InCl_3$; for labeling of autologous leukocyte-rich plasma;

^{111}In- labeled leukocytes
0.2-0.5 mCi; stable for 1 hour.

^{111}In-pentetate (^{111}In-DTPA): 0.020-0.050 mg pentetic acid in 1.5 ml isotonic bicarbonate buffer & 1.5 mCi $^{111}InCl_3$
cisternography, 0.5 mCi;

^{201}Thallium

^{123}Iodide

^{123}I-ioflupane DATSCAN
Diagnostic of Parkinson's disease; 5 mCi

^{123}I-$_{meta}$iodobenzylguanidine (^{123}I-MIBG):
neuroendocrine tumors; 10 mCi;

^{131}I-iodobenzamide (^{123}I-IBZM):

^{131}Iodide

^{131}I-$_{meta}$iodobenzylguanidine (^{131}I-MIBG):
neuroendocrine tumors; 0.5 mCi;

^{131}I-cholesterol

APPENDIX 2: LIST OF REIMBURSED RADIOISOTOPES FOR THERAPEUTIC AND DIAGNOSTIC USE IN BELGIUM

CHAPITRE VI (mise à jour : 01-03-2008)

Conditions de remboursement des radio-isotopes admis.

§ 1. Généralités

L'intervention de l'assurance maladie-invalidité dans le coût des radio-isotopes utilisés à titre thérapeutique ou à titre de diagnostic peut être accordée, pour autant qu'il ne s'agisse pas d'isotopes en sources scellées d'une demi-vie supérieure à quatre mois.

L'intervention de l'assurance calculée comme prévu ci-après, peut être accordée si le traitement est décidé par le médecin et accepté par le patient, et si le radio-isotope est commandé.

Le système du tiers payant peut être appliqué si ce même système est accepté pour les honoraires du traitement même et des consultations.

§ 2. Conditions de remboursement des radio-isotopes utilisés à titre thérapeutique, admis en vertu du groupe de remboursement A-37

L'intervention de l'assurance maladie-invalidité est accordée dans le coût des radio-isotopes utilisés à titre thérapeutique dont la liste suit.

Ces produits sont facturés individuellement par bénéficiaire traité en se référant à la facture du producteur.

Lorsque les radio-isotopes utilisés sont le IODIUM 125 ou le PALLADIUM 103, l'intervention de l'assurance maladie invalidité n'est accordée que s'ils sont administrés dans le cadre d'un traitement de patients atteints d'un carcinome de la prostate de stade T1-T2 avec un taux d'Antigènes prostatiques spécifiques (PSA) inférieur à 20, un Gleason-score inférieur à 8, et un volume prostatique inférieur à 50 ml.

Lorsque le radio-isotope utilisé est une solution de chlorure d'Yttrium 90, l'intervention de l'assurance maladie invalidité n'est accordée que s'il est administré pour le radiomarquage de la spécialité Zevalin pour laquelle doit être introduite simultanément une demande de remboursement pour le traitement en 3ème ligne ou plus, de patients adultes atteints d'un lymphome non hodgkinien (LNH) de type folliculaire à cellules B CD20+, stade III ou IV, en rechute ou réfractaire après un traitement par rituximab.

A cet effet, et dans la mesure où cette démarche n'a pas encore été accomplie au moment de la facture, il y a lieu de joindre au relevé P, une attestation rédigée confidentiellement à l'intention du médecin-conseil de l'organisme assureur par le médecin spécialiste en radiothérapie, responsable du traitement, confirmant que cette indication est rencontrée.

Le prix facturé est la base de remboursement, montant qui est entièrement remboursé par l'assurance.

Liste des isotopes radioactifs médicaux employés à titre thérapeutique pour lesquels l'assurance maladie-invalidité intervient:

A. Sources scellées:

Phosphore 32 (P 32)
Grains d'or (Au 198)
Grains d'iridium 192 (Ir 192)
Grains de tantale 182 (Ta 182)
Grains, sphères et aiguilles d'yttrium 90 (Y 90)
Fils de tantale 182, d'iridium 192 et or 198

B. Radio-éléments et molécules marquées:

Solution Iodure de Na I 125
Solution Iodure de Na I 131
Capsules Iodure de Na I 131
Soluté or colloïdal Au 198
Soluté or colloïdal Au 198 à petites particules
Soluté acide phosphorique P 32
Soluté phosphate de Na P 32
Suspension phosphate de chrome P 32
Complexe colloïdal phosphate de chrome P 32 à petites micelles
Complexe colloïdal phosphate de chrome P 32 à grosses micelles
Complexe colloïdal P 32 + Cr 51
Lipiodol F. marqué à l'I 131.
Lipidiol U.F. marqué à l'I 131
Yttrium 90 en suspension
Phosphate de zirconium P 32 en suspension
Sérum albumine I 131
Strontium 85 ou 85 + 89, en solution ou poudre
Samarium 153 en solution
Iodium 125
Palladium 103
Solution de chlorure d'Yttrium 90

§ 3. Conditions de remboursement des radio-isotopes utilisés à titre diagnostique in vivo, admis en vertu du groupe de remboursement B-205

Tous les radio-isotopes, administrés aux bénéficiaires en vue de poser un diagnostic, peuvent faire l'objet d'un remboursement en catégorie B.

La base sur laquelle est calculée l'intervention de l'assurance, est fixée forfaitairement selon les catégories mentionnées ci-après et est calculée par tranche des montants qui y sont indiqués:

- catégorie à 4,96 €: NaI 131 et NaI 125

- catégorie à 9,92 €: Molécules inorganiques prêtes à l'emploi

- catégorie à 18,59 €: Eluats organiques ou inorganiques à courte vie de générateur utilisés comme tels.

- catégorie à 24,79 €: Eléments sanguins figurés ou protéines plasmatiques du patient, marqués de façon extracorporelle par molécules inorganiques.

- catégorie à 29,75 €: Molécules organiques prêtes à l'emploi.

- catégorie à 37,18 €: Molécules organiques ou inorganiques marquées par isotopes à courte vie produits par générateur.

- catégorie à 49,58 €: I 123 utilisé dans des cas où une exploration de la thyroïde n'a, au cours d'une séance précédente, pas fourni de renseignements suffisants et qu'un examen complémentaire à l'I 123 est dès lors nécessaire.(1)

- catégorie à 49,58 €: I 123 utilisé pour l'exploration de l'atrésie des voies biliaires en pédiatrie.(1)

- catégorie à 49,58 €: I 123 utilisé pour l'exploration du transplant rénal.(1)

- catégorie à 49,58 €: In 111, Ga 67 et Tl 201.

- catégorie à 173,53 €: les radio-isotopes de poids atomique bas O 15, N 13, C 11, F 18 destinés à être utilisés pour effectuer une tomographie à positrons prévue sous les n° s 442971 - 442982 de la nomenclature et dont le médecin-conseil de l'organisme assureur a autorisé le remboursement.

- catégorie à 749,11 €:

ioflupane (DATSCAN ®) I^{123}, utilisé pour effectuer un examen de tomoscintigraphie d'émission monophotonique à l'aide d'une gammacaméra munie d'un collimateur haute résolution calibrée en utilisant le pic d'absorption totale de 159 keV, lorsque cet examen a été prescrit par un médecin spécialiste en neurologie ou en neuropsychiatrie pour réaliser la détection d'une perte de terminaisons neuronales dopaminergiques fonctionnelles dans le striatum de patients présentant un syndrome parkinsonien cliniquement douteux, lorsque toutes les conditions suivantes sont remplies simultanément:

1. l'examen n'a encore jamais été remboursé, suivant la présente réglementation, chez le patient concerné;

2. l'examen concerne un patient adulte et est destiné à établir un diagnostic différentiel entre tremblement essentiel et syndromes parkinsoniens;

3. un médecin spécialiste en neurologie ou en neuropsychiatrie a attesté que l'anamnèse et l'examen clinique ne sont pas suffisamment contributifs pour établir ce diagnostic différentiel;

4. la dose maximale remboursable est de 1 flacon de 2,5 ml ou 185 MBq.

A cet effet, et dans la mesure où cette démarche n'a pas encore été accomplie au moment de la facture, il y a lieu de joindre à la facture intégrée individuelle du patient concerné un rapport médical circonstancié rédigé confidentiellement à l'intention du médecin-conseil de l'organisme assureur par le médecin spécialiste en neurologie ou en neuropsychiatrie, qui confirme que toutes les conditions mentionnées ci-dessus sont rencontrées.

Pour l'application de cette réglementation, on considère comme isotope à courte vie, l'isotope dont la demi-vie est inférieure à 24 h.

Les montants forfaitaires mentionnés ci-devant constituent les moyennes des prix réels et couvrent dès lors tous les frais du radio-isotope utilisé.

L'intervention personnelle du bénéficiaire non hospitalisé est celle prévue, pour la catégorie B (*), à l'article 2.a du chapitre I de l'arrêté royal du 7 mai 1991 précité; elle est calculée par tranche des montants forfaitaires fixée par catégorie susmentionnée.

Le médecin doit mentionner sur l'attestation de soins donnés aussi bien le numéro de catégorie fixé ci-dessus que la dénomination de l'isotope utilisé.

(1) Si l'I 123 est utilisé dans d'autres situations que celles qui sont énumérées, l'isotope sera remboursé sur base de 9,92 € ou 29,75 € suivant qu'il s'agit de l'I 123 inorganique ou de molécules organiques marquées par l'I 123.

(*) Catégorie B: l'intervention personnelle des bénéficiaires est fixée à 15 % du prix de la spécialité pharmaceutique, considéré comme base de remboursement avec un maximum de 6,20 € (7,20 € à partir du 1.1.2008) pour les bénéficiaires visés à l'article 37 § 1er et §19 de la loi susvisée du 14 juillet 1994 et qui ont droit à un remboursement augmenté de l'assurance, et à 25 % du prix de la spécialité pharmaceutique avec un maximum de 9,30 € (10,80 € à partir du 1.1.2008) pour les autres bénéficiaires.

HOOFDSTUK VI (bijwerking : 01-03-2008)

Voorwaarden ter vergoeding van de aangenomen radio-isotopen.

§ 1.Algemeenheden

De tegemoetkoming van de ziekte- en invaliditeitsverzekering in de kosten van therapeutisch of als diagnosemiddel aangewende radio-isotopen kan worden toegestaan voor zover het niet gaat om isotopen als ingekapselde bronnen waarvan de halveringstijd vier maanden overtreft.

De verzekeringstegemoetkoming, berekend zoals hierna bepaald, mag worden uitbetaald zo de behandeling door de geneesheer beslist en door de patiënt aanvaard is, en zo het radio-isotoop is besteld.

De derde betalersregeling mag worden toegepast zo diezelfde regeling is aanvaard voor de honoraria der behandeling zelf en der raadpleging.

§ 2. Voorwaarden voor de vergoeding van de therapeutisch aangewende radio-isotopen die zijn aangenomen krachtens de vergoedingsgroep A-37

De tegemoetkoming van de ziekte- en invaliditeitsverzekering wordt toegestaan in de kosten van de therapeutisch aangewende geneeskundige radio-isotopen waarvan de lijst volgt.

Deze producten worden individueel gefactureerd per behandelende rechthebbende onder referte naar de factuur van de voortbrenger.

Indien de gebruikte radio-isotopen IODIUM 125 of PALLADIUM 103 zijn, wordt de tussenkomst van de ziekte- en invaliditeitsverzekering enkel toegestaan indien ze toegediend zijn in het kader van een behandeling van patiënten met een prostaatcarcinoom stadium T1-T2 met een gehalte prostaat specifiek antigen (PSA) lager idan 20, een Gleason-score lager dan 8 en een prostaatvolume lager dan 50 ml.

Indien het gebruikte radio-isotoop een oplossing is van Yttrium 90 chloride, wordt de tussenkomst van de ziekte- en invaliditeitsverzekering enkel toegestaan indien ze gebruikt wordt voor de radioactieve labeling van de specialiteit Zevalin waarvoor simultaan een aanvraag voor vergoeding moet ingediend worden, voor de behandeling in 3de lijn of meer, van volwassen patiënten met een CD20+ folliculair B-cel non-Hodgkinlymfoom (NHL) stadium III of IV, die in recidief zijn na, of refractair zijn aan een behandeling met rituximab.

Indien dit nog niet is gebeurd bij de facturering, moet hiertoe bij de staat P een vertrouwelijk attest worden gevoegd voor de adviserend geneesheer van de verzekeringsinstelling, opgesteld door de geneesheer-specialist in de radiotherapie, verantwoordelijk voor de behandeling, waarin hij de behandeling van de voornoemde indicatie bevestigt.

De gefactureerde prijs is de basis van tegemoetkoming, bedrag dat volledig door de verzekering wordt vergoed.

Lijst van de therapeutisch aangewende geneeskundige radioactieve isotopen waarvoor de ziekte- en invaliditeitsverzekering tegemoetkomt:

A. Ingekapselde bronnen:

Fosfor 32 (P 32)
Goud 198, korrels (Au 198)
Iridium 192, korrels (Ir 192)
Tantalium 182, korrels (Ta 182)
Yttrium 9O, korrels, bolletjes en naalden (Y 9O)
Tantalium 182, Iridium 192 en goud 198-draad

B. Radio-elementen en gemerkte moleculen:

Oplossing van Na-iodide I 125
Oplossing van Na-iodide I 131
Capsules Na-iodide I 131
Oplossing van colloïdaal goud Au 198
Oplossing van colloïdaal goud Au 198, kleine deeltjes
Oplossing van fosforzuur P 32
Oplossing van Na-fosfaat P 32
Suspensie van chroomfosfaat P 32
Colloïdaal complex van chroomfosfaat P 32, kleine micellen
Colloïdaal complex van chroomfosfaat P 32, grote micellen
Colloïdaal complex P 32 + Cr 51
Met I 131 gemerkte Lipiodol F.
Met I 131 gemerkte lipiodol U.F.
Yttrium 9O in supensie
Zirconiumfosfaat P 32 in suspensie
Serum Albumine I 131
Strontium 85 of 85 + 89, in oplossing of poeder
Samarium 153 in oplossing.
Iodium 125
Palladium 103
Oplossing van Yttrium 90 chloride

§ 3.Voorwaarden voor de vergoeding van de diagnostisch in vivo aangewende radio-isotopen die zijn aangenomen krachtens de vergoedingsgroep B-205

Alle radio-isotopen, toegediend aan de rechthebbenden om een diagnose te stellen, mogen worden vergoed in categorie B.

De basis waarop de verzekeringstegemoetkoming wordt berekend, is forfaitair vastgesteld volgens de hierna vermelde categorieën en wordt berekend per tranche van de opgegeven bedragen:

- categorie à 4,96 €: NaI 131 en NaI 125

- categorie à 9,92 €: Anorganische molekulen klaar voor gebruik.

- categorie à 18,59 €: Als zodanig aangewende kortlevende organische of anorganische generatoreluaten.

- categorie à 24,79 €: Gefigureerde bloedelementen of plasmaproteïnen van de patiënt, extracorporeaal gemerkt met anorganische molekulen.

- categorie à 29,75 €: Gebruiksklare organische molekulen.

- categorie à 37,18 €: Organische of anaorganische molekulen gemerkt met kortlevende isotopen geproduceerd door generator.

- categorie à 49,58 €: I 123 aangewend in gevallen waar een exploratie van de schildklier in een vorige vacatie onvoldoende inlichtingen bezorgde zodat een aanvullend onderzoek met I 123 aangewezen is.(1)

- categorie à 49,58 €: I 123 aangewend voor de exploratie naar galwegen-atresie in de pediatrie.(1)

- categorie à 49,58 €: I 123 aangewend voor de exploratie van de transplantnier.(1)

- categorie à 49,58 €: In 111, Ga 67 en Tl 201.

- categorie à 173,53 €: de radio-isotopen met een laag atoomgewicht O 15, N 13, C 11, € 18 die worden gebruikt om een positronentomografie tot stand te brengen die voorzien is onder nrs. 442971 - 442982 van de nomenclatuur en waarvoor de adviserend geneesheer van de verzekeringsinstelling de vergoeding heeft gemachtigd.

- categorie à 749,11 €:

ioflupane (DATSCAN ®) I^{123}, gebruikt om een single photon emission tomoscintigrafie uit te voeren met behulp van een gammacamera voorzien van een hogeresolutiecollimator, gecalibreerd door gebruikt te maken van de totale absorptiepiek van 159 keV, als dit onderzoek is voorgeschreven geweest door een arts gespecialiseerd in neurologie of in neuropsychiatrie, om een verlies van functionele dopaminerge neuronale uiteinden in het striatum bij patiënten met een klinisch onzeker parkinsonsyndroom te detecteren als alle volgende criteria gelijktijdig worden vervuld:

1. het onderzoek is nog nooit terugbetaald geweest volgens de huidige reglementering bij de betrokken patiënt;

2. het onderzoek betreft een volwassen patiënt en is bestemd om een differentiële diagnose te maken tussen essentiële tremor en parkinsonsyndromen;

3. de arts gespecialiseerd in neurologie of neuropsychiatrie attesteert dat de anamnese en het klinisch onderzoek niet voldoende bijdragen tot deze differentiële diagnose;

4. de maximum terugbetaalde dosis is 1 flacon van 2,5ml of 185 MBq.

Hiertoe, en in de mate dat dit nog niet is gebeurd op het ogenblik van facturatie, is er reden om aan de factuur van de individuele patiënt ten behoeve van de adviserend geneesheer van het verzekeringsorganisme door de arts gespecialiseerd in neurologie of neuropsychiatrie, een omstandig vertrouwelijk medisch rapport toe te voegen dat bevestigt dat aan alle hiervoor opgesomde voorwaarden is voldaan.

Voor de toepassing van deze reglementering wordt als kortlevende isotoop beschouwd, het isotoop waarvan de halveringstijd minder dan 24 u. bedraagt.

De hiervoren vermelde forfaitaire bedragen zijn maken gemiddelden van de werkelijke prijzen en dekken derhalve alle kosten van de aangewende radio-isotoop.

Het persoonlijk aandeel van de niet in een ziekenhuis opgenomen rechthebbende is dat waarin voor de categorie B (*) is voorzien in artikel 2.a van hoofdstuk I van vorenvermeld koninklijk besluit van 7 mei 1991; het wordt berekend per tranche van de forfaitaire bedragen die is vastgesteld per hiervoren vermelde categorie.

De geneesheer dient op het getuigschrift voor verstrekte hulp zowel het hiervoren vastgestelde categorienummer als de benaming van het aangewende isotoop te vermelden.

(1) Indien I 123 in andere dan de opgesomde gevallen wordt aangewend zal het isotoop worden vergoed op basis van 9,92 € of 29,75 € naargelang het om anorganische I 123 of met I 123 gemerkte organische molekulen gaat.

(*) Categorie B: het persoonlijk aandeel van de rechthebbenden wordt vastgesteld op 15 % van de prijs van de farmaceutische specialiteit die als vergoedingsbasis geldt, met een maximum van 6,20 € (7,20 € vanaf 1.1.2008), voor de rechthebbenden bedoeld in artikel 37 §1 en §19 van de voornoemde wet van 14 juli 1994 die recht hebben op een verhoogde verzekeringstegemoetkoming, en op 25 % van de prijs van de farmaceutische specialiteit met een maximum van 9,30 € (10,80 € vanaf 1.1.2008), voor de andere rechthebbenden.

APPENDIX 3: TARIFFS FOR NUCLEAR MEDICINE PROCEDURES IN THE NETHERLANDS

I Reimbursement of diagnostic procedures

Code	€	Description
120001	184,1	VENTRIKELDRAINFUNCTIE-ONDERZOEK.
120003	125,8	HERSENPERFUSIEONDERZOEK (STATISCH, HERSENDOOD).
120005	360,60	KWANTITATIEVE HERSENDOORBLOEDING (ML/MIN/100G WEEFSEL).
120006	418,60	LIQUORCIRCULATIEONDERZOEK.
120010	154,4	SPEEKSELKLIERONDERZOEK (AL OF NIET MET INTERVENTIE).
120011	301,6	SCHILDKLIER DISCHARGETEST.
120012	154,4	SCHILDKLIER UPTAKE-METING.
120013	150,8	SCHILDKLIERSCINTIGRAFIE.
120014	360,6	BIJSCHILDKLIERONDERZOEK.
120015	184,1	TRAANWEGONDERZOEK.
120027	22,20	DOELGERICHTE CONSULTATIE VAN EEN ONDERSTEUNEND SPECIALIST DOOR EEN POORTSPECIALIST BIJ EEN AL GEOPEN
120030	184,10	STATISCH SKELETONDERZOEK.
120031	184,10	MEERFASEN SKELETONDERZOEK.
120033	154,40	SKELETDENSITOMETRIE GEHELE LICHAAM. HIERONDER VALT NIET HET ONDERZOEK MET DEXA-APPARATUUR.
120034	92,50	SKELETDENSITOMETRIE HEUPEN. NAAST DEZE VERRICHTING KAN NIET VERRICHTING 120033 WORDEN GEDECLAREERD.
120035	92,50	SKELETDENSITOMETRIE LUMBALE WERVELKOLOM. NAAST DEZE VERRICHTING KAN NIET VERRICHTING 120033 WORDEN GEDECLAREERD
120036	125,80	GEWRICHTSONDERZOEK.
120043	243,10	EJECTIEFRACTIE L.V. MET WANDBEWEGINGSANALYSE. NAAST DEZE VERRICHTING KAN NIET VERRICHTING 120045 WOR
120044	243,10	EJECTIEFRACTIE L.V. EN R.V. MET WANDBEWEGINGSANALYSE. NAAST DEZE VERRICHTING KAN NIET VERRICHTING 12
120045	217,30	EJECTIEFRACTIEMETING BIJ MEERDERE INSPANNINGSNIVEAU'S. NAAST DEZE VERRICHTING KUNNEN NIET DE VERRICH
120046	154,40	CARDIALE SHUNTMETING.
120047	184,10	FIRST-PASS-HARTONDERZOEK.
120060	184,10	LONGPERFUSIEONDERZOEK.
120061	184,10	LONGVENTILATIEONDERZOEK MET EDELGASSEN OF AEROSOLEN.
120063	184,10	MUCOCILIAIR TRANSPORT IN DE LONGEN.
120064	184,10	MUCOCILIAIR TRANSPORT IN DE NEUS.
120065	184,10	SLOKDARMBEWEGINGSONDERZOEK.
120069	243,10	GASTRO-OESOFAGEALE REFLUXONDERZOEK (066).
120070	301,60	MAAGONTLEDIGINGSONDERZOEK (063).
120071	418,60	MAAGONTLEDIGINGSONDERZOEK MET MEERDERE TRACERS.
120072	301,60	ONTLEDIGINGSONDERZOEK VAN ONDERDELEN VAN DE MAAG.
120073	243,10	MAAGSLIJMVLIESONDERZOEK (064).

120076	360,60	ONDERZOEK NAAR BLOEDVERLIES IN DE TRACTUS DIGESTIVUS GEDURENDE ÉÉN DAG (091).
120077	418,60	ONDERZOEK NAAR BLOEDVERLIES IN DE TRACTUS DIGESTIVUS GEDURENDE MEERDERE DAGEN (091).
120080	184,10	LEVER- EN MILTONDERZOEK.
120081	243,10	MILTONDERZOEK MET GEDENATUREERDE RODE CELLEN (082).
120082	301,60	GALAFVLOED ONDERZOEK (081).
120084	360,60	ASCITESONDERZOEK.
120090	243,10	LYMFEKLIERONDERZOEK MET AFVLOEDMETING (092).
120091	301,60	PARASTERNAAL LYMFEKLIERONDERZOEK.
120092	360,60	SCHILDWACHTKLIERPROCEDURE MET BIJBEHORENDE BEELDVORMING.
120093	451,80	SCHILDWACHTKLIERPROCEDURE MET BIJBEHORENDE BEELDVORMING EN OK.
120094	184,10	MAMMASCINTIGRAFIE.
120095	301,60	BEENMERGONDERZOEK (093).
120100	184,10	NIERONDERZOEK STATISCH (DMSA).
120101	243,10	RENOGRAFIE (102).
120102	301,60	RENOGRAFIE MET FARMACOLOGISCHE INTERVENTIE.
120103	243,10	VESICO-URETERALE REFLUXONDERZOEK.
120104	360,60	RENOGRAFIE GECOMBINEERD MET V-U REFLUX BEPALING.
120106	478,10	RENOGRAFIE MET KLARINGSONDERZOEK.
120107	154,40	ONDERZOEK SCROTALE DOORBLOEDING (105).
120110	536,10	ONDERZOEK NEURO-ECTODERMAAL WEEFSEL GEDURENDE ÉÉN DAG.
120111	595,60	ONDERZOEK NEURO-ECTODERMAAL WEEFSEL GEDURENDE MEERDERE DAGEN.
120112	360,60	BIJNIERSCHORSONDERZOEK
120113	595,60	BIJNIERMERGONDERZOEK (INCLUSIEF EVENTUELE UPTAKE-METING).
120130	536,10	RECEPTORENONDERZOEK GEDURENDE ÉÉN DAG
120131	595,60	RECEPTORENONDERZOEK GEDURENDE TWEE DAGEN
120150	154,40	FLEBOGRAFIE BOVENSTE OF ONDERSTE EXTREMITEITEN
120152	536,10	TUMORLOKALISATIE MBV PEPTIDEN E.D. (153).
120153	360,60	TUMORLOKALISATIE MBV GA: TL: V DMSA E.D. (156).
120154	653,60	ABCES/ONTSTEKINGSLOKALISATIE MET BEHULP VAN GELABELDE LEUKO´S.
120156	243,10	ORGAANPERFUSIE (VOOR ZOVER NIET APART VERMELD) (155).
120160	125,80	GFR (SINGLE SHOT-METHODE).
120161	125,80	ERPF (SINGLE SHOT-METHODE).
120162	536,10	GFR EN ERPF (CONSTANTE INFUSIE-METHODE).
120170	385,30	PLASMAVOLUMEBEPALING.
120171	444,80	ERYTROCYTENVOLUMEBEPALING.
120172	150,80	EXTRACELLULAIRVOLUMEBEPALING.
120173	243,10	EIWITVERLIESBEPALING VIA DE TRACTUS DIGESTIVUS.
120174	150,80	ERYTROCYTENOVERLEVINGSDUURBEPALING.
120175	184,10	THROMBOCYTENOVERLEVINGSDUURBEPALING.
120176	268,30	SCHILLING-TEST.
120177	301,60	IJZERKINETIEK.
120178	301,60	BEPALING GALZUURMETABOLISME.
120179	59,20	C14-UREUMADEMTEST.

120203	418,60	SPECT VAN HERSENDOORBLOEDING.
120205	947,60	SPECT VAN RECEPTOREN IN HERSENEN.
120230	150,80	SPECT VAN SKELET DETAIL.
120240	243,10	SPECT VAN MYOCARD RUST.
120241	334,80	SPECT VAN MYOCARD INSPANNING MET STRESS-TEST.
120244	301,60	SPECT VAN MYOCARD VITALITEIT
120245	418,60	SPECT VAN HARTKAMERS ECG-GETRIGGERD, RUST MET EF- BEREKENING (244).
120246	511,30	SPECT VAN HARTKAMERS ECG-GETRIGGERD MET EF-BEREKENING, INSPANNING EN STRESS-TEST (244).
120255	243,10	SPECT VAN THORAX.
120260	243,10	SPECT VAN LONGPERFUSIE. NAAST DEZE VERRICHTING KAN NIET VERRICHTING 120261 WORDEN GEDECLAREERD.
120261	478,10	SPECT VAN LONGVENTILATIE MET PERFUSIE. NAAST DEZE VERRICHTING KAN NIET VERRICHTING 120260 WORDEN GEDECLAREERD
120280	243,10	SPECT VAN ABDOMEN.
120300	243,10	SPECT VAN NIERSCHORS.
120310	595,60	SPECT RECEPTORENONDERZOEK ÉÉN DAG.
120311	653,60	SPECT RECEPTORENONDERZOEK MEERDERE DAGEN.
120412	22,20	CONSULT, NIET GEVOLGD DOOR EEN NUCLEAIR GENEESKUNDIGE BEHANDELING.
120413	22,20	CONTROLE BIJ NUCLEAIR GENEESKUNDIGE BEHANDELING VAN ZIEKTE, PER KEER.
120500	947,60	PET PARTIEEL (NEUROLOGISCH, CARDIOLOGISCH).
120501	1.340,50	PET WB (WHOLE BODY), ONCOLOGIE.

II Reimbursement of therapeutic procedures

Code	€	Description
120400	368,00	BEHANDELING HYPERTHYREOIDIE MET I-131.
120401	368,00	BEHANDELING GROOT STRUMA MET I-131.
120402	544,50	BEHANDELING SCHILDKLIERTUMOREN MET I-131 (401).
120403	309,50	BEHANDELING SYNOVIA MET RADIOACTIEF COLLOID PER GEWICHT.
120404	544,50	THERAPIE PLEURA-EXSUDAAT/ASCITES MET RADIOACTIEF COLLOID.
120403	309,50	BEHANDELING SYNOVIA MET RADIOACTIEF COLLOID PER GEWICHT.
120404	544,50	THERAPIE PLEURA-EXSUDAAT/ASCITES MET RADIOACTIEF COLLOID.
120405	485,00	BEHANDELING POLYCYTHAEMIA VERA MET P-32 (402).
120406	2.482,00	BEHANDELING PIJNLIJKE BOTMETASTASEN MET SR-89 (405).
120407	1.014,00	BEHANDELING PIJNLIJKE BOTMETASTASEN MET RE-186 (406).
120408	1.014,00	BEHANDELING PIJNLIJKE BOTMETASTASEN MET SA-153.
120410	2.482,00	BEHANDELING NEURO-ENDOCRIENE TUMOREN (MIBG-HOOG) (407).

APPENDIX 4: ESTIMATED NATIONAL AVERAGE REIMBURSEMENT TARIFFS FOR DIAGNOSTIC PROCEDURES WITH RADIOISOTOPES IN ITALY (2007)

Code	**Scintigrafia tiroidea e paratiroidea con studio funzionale radioisotopico**	
92.01.1	Captazione tiroidea	€ 44,98
92.01.2	Scintigrafia tiroidea con captazione con o senza prove farmacologiche	€ 46,12
92.01.3	Scintigrafia tiroidea	€ 33,36
92.01.4	Scintigrafia tiroidea con traccianti positivi	€ 179,73
92.13	Scintigrafia delle paratiroidi. Con tecnica di sottrazione incluso scintigrafia della tiroide	€ 191,04
	Scintigrafia epatica e studio funzionale radioisotopico	
92.02.1	Scintigrafia epatica (3 proiezioni). In caso di contemporanea esecuzione di tomoscintigrafia codificare anche 92.02.5	€ 64,56
92.02.2	Scintigrafia epatica per ricerca di lesioni angiomatose. In caso di contemporanea esecuzione di tomoscintigrafia codificare anche 92.02.5	€ 115,01
92.02.3	Scintigrafia sequenziale epatobiliare, inclusa colecisti, con o senza prove farmacologiche, con o senza misurazione della funzionalità della colecisti	€ 103,55
92.02.4	Scintigrafia epatica con indicatori positivi. In caso di contemporanea esecuzione di tomoscintigrafia codificare anche 92.02.5	€ 154,94
92.02.5	Tomoscintigrafia (SPET) epatica (successiva a esame planare) in corso di esame planare con unica somministrazione del tracciante	€ 25,93
	Scintigrafia renale e studio funzionale radioistopico	
92.03.1	Scintigrafia renale. In caso di contemporanea esecuzione di tomoscintigrafia codificare anche 92.03.5	€ 56,81
92.03.2	Scintigrafia renale con angioscintigrafia (in corso di scintigrafia renale con unica somministrazione di tracciante)	€ 22,98
92.03.3	Scintigrafia sequenziale renale (studio sequenziale della funzione renale senza o con prove farmacologiche), incluso misura del filtrato glomerulare o della portata renale plasmatica	€ 112,33
92.03.4	Studio del reflusso vescico-ureterale. Mediante cistoscintigrafia minzionale diretta	€ 74,42
92.03.5	Tomoscintigrafia (SPET) renale (successiva a esame planare con unica somministrazione di radiofarmaco)	€ 41,26
	Scintigrafia gastrointestinale e studio funzionale	
92.04.1	Scintigrafia sequenziale delle ghiandole salivari con studio funzionale	€ 63,89
92.04.2	Studio del transito esofago-gastro-duodenale	€ 51,65
92.04.3	Studio del reflusso gastro-esofageo o duodeno-gastrico	€ 92,96
92.04.4	Valutazione delle gastroenterorragie	€ 103,29
92.04.5	Studio della permeabilità intestinale	€ 61,46
	Scintigrafia cardiovascolare ed emopoietica e studio funzionale radioisotopico	
92.05.1	Scintigrafia miocardica di perfusione, a riposo e dopo stimolo (fisico o farmacologico), studio quantitativo	€ 187,01
92.05.2	Scintigrafia miocardica con indicatori positivi di lesione. In caso di contemporanea esecuzione di tomoscintigrafia codificare anche 92.09.3	€ 51,65
92.05.3	Angiocardioscintigrafia di primo passaggio (first pass): studi multipli del pool ematico cardiaco first pass, a riposo e durante stimolo (fisico o farmacologico), studio del movimento di parete e frazione di eiezione, analisi quantitativa	€ 98,13
92.05.4	Angiocardioscintigrafia all'equilibrio (gating): studi multipli del pool ematico cardiaco all'equilibrio, a riposo e dopo stimolo (fisico e/o farmacologico), studio del movimento di parete e frazione di eiezione, analisi quantitativa	€ 129,11
92.05.5	Scintigrafia splenica	€ 90,12
92.05.6	Scintigrafia del Midollo Osseo total body	€ 108,46

	Altri studi di funzione con radioisotopi	
92.09.1	Tomoscintigrafia miocardica (PET) di perfusione, a riposo o dopo stimolo	€ 1.071,65
92.09.2	Tomoscintigrafia miocardica (SPET) di perfusione, a riposo o dopo stimolo	€ 134,80
92.09.3	Tomoscintigarfia miocardica con indicatori di lesione in corso di esame planare con indicatori di lesione, con unica somministrazione di radiofarmaco	€ 41,26
92.09.4	Determinazione del volume plasmatico o del volume ertitrocitario	€ 46,22
92.09.5	Studio di sopravvivenza degli eritrociti, cinetica differenziale per organo/tessuto (fegato, milza)	€ 179,31
92.09.6	Studio completo della ferrocinetica	€ 143,58
92.09.7	Studio della cinetica delle piastrine o dei leucociti, con o senza localizzazione differenziale per organo/tessuto	€ 221,25
	Scintigrafia cerebrale	
92.11.1	Scintigrafia cerebrale statica	€ 98,13
92.11.2	Scintigrafia cerebrale con angioscintigrafia, studio completo	€ 126,27
92.11.3	Valutazione delle derivazioni liquorali	€ 129,11
92.11.4	Determinazione e localizzazione perdite di LCR	€ 206,58
92.11.5	Tomoscintigrafia cerebrale (SPET)	€ 238,81
92.11.6	Tomoscintigrafia cerebrale (PET), studio qualitativo	€ 939,95
92.11.7	Tomoscintigrafia cerebrale (PET), studio quantitativo	€ 1.071,65
	Scintigrafia delle ossa	
92.14.1	Scintigrafia ossea o articolare segmentaria	€ 57,84
92.14.2	Scintigrafia ossea o articolare segmentaria polifasica	€ 78,35
92.14.3	Tomoscintigrafia ossea (SPET) in corso di esame planare con unica somministrazione di radiofarmaco	€ 36,15
	Scintigrafia polmonare	
92.15.1	Scintigrafia polmonare perfusionale (6 proiezioni)	€ 68,48
92.15.2	Scintigrafia polmonare ventilatoria	€ 198,63
92.15.3	Studio quantitativo differenziale della funzione polmonare (eventuale aggiunta a scintigrafia perfusionale o ventilatoria 92.15.1 - 92.15.2)	€ 22,98
92.15.4	Scintigrafia polmonare con indicatore positivo	€ 169,45
92.15.5	Tomoscintigrafia polmonare (SPET), in corso di scintigrafia polmonare con unica somministrazione di tracciante	€ 34,71
	Scintigrafia del sistema linfatico	
92.16.1	Scintigrafia linfatica e linfoghiandolare segmentaria	€ 110,52
	Scintigrafia Total Body	
92.18.1	Scintigrafia globale corporea con indicatori positivi	€ 213,55
92.18.2	Scintigrafia ossea o articolare	€ 113,10
92.18.3	Ricerca di metastasi di tumori tiroidei	€ 136,60
92.18.4	Scintigrafia globale corporea con cellule autologhe marcate	€ 251,57
92.18.5	Scintigrafia globale corporea con traccianti immunologici o recettoriali	€ 413,17
92.18.6	Tomoscintigrafia globale corporea (PET)	€ 1.071,65
	Scintigrafia di altre sedi	
92.19.1	Scintigrafia surrenalica corticale	€ 259,00
92.19.2	Scintigrafia surrenalica midollare	€ 293,45
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92.19.4	Scintigrafia delle trombosi venose (venogramma)	
92.19.5	Angioscintigrafia (angiografia, venografia radioisotopica)	€ 86,25
92.19.6	Scintigrafia segmentaria dopo scintigrafia total body (con o senza indicatori positivi, cellule autologhe marcate, traccianti immunologici o recettoriali)	€ 24,79
92.19.7	Scintigrafia segmentaria con indicatori positivi	€ 169,40
92.19.8	Tomoscintigrafia (SPET) con indicatori positivi in corso di esame planare con unica somministrazione di radiofarmaco	€ 36,15

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