Radionuclide therapy practice and facilities in Europe

C.A. Hoefnagel, S.E.M. Clarke, M. Fischer, J.F. Chatal, V.J. Lewington, S.Nilsson, L. Troncone, M.R. Vieira
(EANM Radionuclide Therapy Committee)

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Introduction

Therapeutic nuclear medicine is a systemic, non-invasive treatment modality which is characterised by the selective delivery of radiation doses to target tissues (tumours or organs). Its limited toxicity and long-term effects compare favourably with those of chemotherapy and external beam radiotherapy.

For several benign disorders radionuclide therapy provides an alternative to surgical or medical treatment. For the treatment of malignant diseases this modality combines the advantage of being selective (like brachytherapy or external beam radiotherapy) with that of being systemic (like chemotherapy).

Limiting factors are that not all tumours show sufficient uptake and retention of the radiopharmaceutical, national legislation, the restiricted availability of the necessary facilities and finances and the limited commercial availability of therapeutic compounds. Nevertheless, the role of therapeutic nuclear medicine is expanding, as more radiopharmaceuticals are being developed for therapeutic use, new indications are emerging and results are improving. Based upon current indications and legislation it has been calculated that in Germany by the year 2000 one isolation bed will be required per 20000–40000 inhabitants.

Using a questionnaire the EANM Task Group Radionuclide Therapy in 1993 collected data on the current practice of radionuclide therapy in European countries. Subsequently, at the request of the EANM Executive Committee, the EANM Radionuclide Therapy Committee has made an inventory of the distribution of facilities for radionuclide therapy and undertaken an assessment of the total number of patients treated throughout Europe and of the types of treatment provided, with the aim of supporting the development of policy to adjust the available capacity to the needs by the year 2000. For this purpose, a second, more detailed questionnaire was sent out to the members and national advisors of the Committee (see below), who gathered the data for each country that was a member of the EANM at the time.

The EANM Radionuclide Therapy Committee wishes to thank all participating colleagues for their contributions and to inform them and all EANM members of the findings.

Corresponding author: Dr. C.A. Hoefnagel, Department of Nuclear Medicine, The Netherlands Cancer Institut, Antoni van Leeuwenhoek Ziekenhuis, Plesmanlaan 121,1066 CX Amsterdam, The Netherlands

Clinical practice

The first questionnaire (1993) focussed on the basic standards for radionuclide therapy, e.g. responsible physicians, level of training and experience, licensing, storage of radioactive waste, and mechanisms to report adverse effects, and on the therapeutic use of iodine-131 in particular. The questionnaire was sent out to 21 countries and replies were received from 16 national advisors or Task Group members. Table 1 shows the questions and the answers obtained for each country.

It is apparent that there are still considerable variations between countries in the basic conditions for radionuclide therapy. Although a nuclear medicine physician is generally authorised to give this form of treatment, in some countries other specialists are carrying out these treatments, including radiotherapists in five countries, endocrinologists in four, other trained specialists in one and any doctor or physicist in another country.

Although most countries specify the requirements for physicians to be trained in therapeutic nuclear medicine, the type and level of training varies. Specific licensing of doctors for therapy is required only in the United Kingdom; in other countries the level of expertise is generally unspecified, although varying minimum required levels of experience are stated. However, in 15/16 countries a licensing process is involved with respect to the department and/or the physician.

In most countries patients treated with ^{131}I for thyrotoxicosis are not admitted to hospital, exception being Austria, the Czech Republic and Slovakia, Germany, Hungary and The Netherlands. The level of the administered dose of ^{131}I, above which patients must be admitted to isolation facilities varies from 1.1 to 30 mCi (40–1110 MBq).

Routine detailed dosimetry is only performed in Austria, the Czech Republic and Slovakia, and Germany; in three other countries semiquantitative estimates are routinely performed. In 14/16 countries there is a legal re-

Table 1. Data on current radionuclide therapy practice in European countries

Country	Question[a]							
	1	2	3	4	5	6	7	8
Austria	Nucl. medicine	Int. medicine or radiology (5 yrs) + nucl. medicine (3 yrs)	>100 therapies under instruction	Yes ?	No	Yes	Yes	No
Belgium	Since 1985 only nuclear med. specialists	Included in nucl. med. specialist training	>30 treatments	Yes nucl. med. specialist with permission from Min.of Health	No 15 mCi	No	Yes	No (EANM proposal to be instigated)
Czechia Republic + Slovakia	Nucl. medicine	Nucl. medicine with regard to endocrinology	2nd specialisation in nucl. med.	Yes ?	Yes	Yes	Yes	Yes (yearly)
France	Nucl. medicine	Nucl. medicine spec. (4 yrs) 1.5 yrs in NM dept.	No special experience	Dept., but named doctor	No 20 mCi	Usually not	Only at beginning	Not really
Germany	Nucl. medicine	NM consultant 5 yrs training incl. therapy 1 yr and int. med 1 yr	As in 2	Dept. +/- doctor	Yes	Yes	Yes	Yes (EANM)
Hungary	Nucl. medicine	Nucl. medicine (2 yrs)	NM Board exam.	Yes ?	Yes	No	Yes (Natl. Pharm Inst)	Yes
Ireland	Nucl. medicine Radiotherapist Endrocrinologist	Medical consultant as in 1	Unspecified “quantity” of experience	Yes doctor	Yes 15 mCi	No	Yes	Yes (Nat.Drugs Adv.Board)
Italy	Nucl. medicine Radiotherapist	NM/RT Consultant 4 yrs training	As in 2	Yes Dept.	No 10–15 mCi is current practice	Yes Act/weight	Yes	Yes (Italian SNM and EANM)
The Netherlands	Nucl. medicine	NM consultant 4 yrs training, incl. therapy and int. med. (1 yr)	As in 2	? Dept. Yes	Yes 1 mCi	Semi-quant.	Yes	Yes (EANM)
Norway	Any	MD	None	Yes Dept.	No 30 mCi	No (Uptake)	No	Yes (EANM)
Portugal	Nucl. medicine	NM consultant (4 yrs)	3 months in dept. doing therapy	No	No 15 mCi	No	Yes	No Port. NMS Initiative

Table 1. (continued)

Country	Question[a]							
	1	2	3	4	5	6	7	8
Slovenia	Nucl. medicine	NM consultant or internal med. + nucl. med. (1 yr)	Not specified	Dept.	No 15 mCi	No	Recently accepted; no facilities yet	Yes (EANM)
Sweden	Oncologists	Therapy optional will change R. physics R. therapy R. biology	No specific experience req'd. (under review)	Dept.	No 15 mCi	Semi-quant.	No	General Agency for Medical Drugs
Switzerland	Nucl. medicine physicians + other trained specialists	Radiation protection 3/52 course+exam. or nuclear medicine specialist degree	6/12 months experience in a nuclear medicine therapy unit	Yes Diploma	No 5 mCi	Only prior to discharge	Short lived in dept.	Yes to Radiation Protection in Ministry of Health
Turkey	Nucl. medicine	3 yrs NM at univ. hospital	As in 2	Yes Dept.	No 30 mCi	Usually not	Yes	No
United Kingdom	Nucl. medicine Radiotherapist Trained endocrinologist	Unspecified period of training + experience	Practical experience + ARSAC licence	Yes Dept./doctor	No 15/30 mCi	Usually not	Yes above locally agreed level	Yes (EANM)

[a] Questions were as follows:
1) Which groups are entitled to give radionuclide therapy?
2) What training is required?
3) What experience is required?
4) Is a license or special permit required?
5) Must all patients be admitted for radioiodine therapy of thyrotoxicosis; if not, above what administered dose is admission mandatory?
6) Is detailed dosimetry usually performed?
7) Is there a legal rerquirement to store radioactive waste?
8) Is there a mechanism for reporting adverse reactions to radiopharmaceuticals?

quirement to store radioactive waste; the situation is different in Norway and Sweden.

Although in most countries a mechanism to report adverse reactions to radiopharmaceuticals is in place, in practice it is hardly ever used.

Facilities

In a second questionnaire 23 countries that were members of the EANM at the time were surveyed to determine the numbers of therapy centres, isolation beds, and patients treated by radionuclide therapy, as well as the indications and amount of administered activity per year.

Data have been received from 20 countries having a combined population of 478 million. In these countries 630 centres are involved in radionuclide therapy (see Table 2). More detailed information was obtained from 18 countries, in which a total of 1520 dedicated beds for radionuclide therapy are available to a population of 434 million, i.e. 1 isolation bed per 285 526 inhabitants, a much lower density than would be required according to the scenario stated above. Table 2 shows the number of isolation beds in individual countries in relation to the required density.

For a number of countries information was provided about the size of the therapy centres. This information showed that the majority of centres have a limited capacity (1–3 beds), except in Austria and Germany, where larger facilities exist (Table 3).

Table 2. Distribution of radionuclide therapy centres in Europe and availability of isolation facilities per country in order of relative prevalence

Country	Population	Therapy centres	Isolation beds	Density 1 bed per *N*
German scenario required by 2000	80 million		2000	40000
Germany	76 million	121	791	96000
Austria	8 million	10	58	138000
Switzerland	6 million	22	43	140000
Czech Republic + Slovakia	10 million	6	70	143000
Slovenia	2 million	5	12	167000
The Netherlands	15.3 million	30	66	232000
Norway	4 million	21	16	250000
Hungary	11 million	10	36	306000
France	55 million	60	140	393000
Italy	57 million	75	120	475000
Israel	5 million	7	9	556000
United Kingdom	56 million	102	84	667000
Greece	10.5 million	16	11	955000
Ireland	4 million	2	4	1000000
Portugal	10 million	4	9	1111000
Spain	35 million	60	30	1167000
Turkey	60 million	11	21	2857000
Sweden	9 million	23	0	–
Poland	39 million	24	n.a	n.a.
Denmark	5 million	21	n.a.	n.a.
Total	478 million	630	1520	286000

n.a., Not available

Table 3. Number of isolation beds available in 318 therapy centres in 15 European countries

Country	1–3 beds	4–7 beds	8–12 beds	>12 beds
Austria	4	2	3	1
Czech Republic + Slovakia	–	–	3	3
Germany	33	51	21	16
Hungary	7	1	2	–
Ireland	2	–	–	–
Israel	7	–	–	–
Italy	17	10	4	–
The Netherlands	21	6	–	–
Norway	8	–	–	–
Portugal	3	1	–	–
Slovenia	1	–	1	–
Spain	25	–	–	–
Switzerland	10	5	–	–
Turkey	5	1	–	–
United Kingdom	35	8	–	–
Total	178 (56%)	85 (26.7%)	35 (11%)	20 (3.3%)

Table 4. Number of patients receiving radionuclide therapy in 18 European countries

Country	Patients treated	Patients/million inhabitants
Austria	2300	288
Czech Republic + Slovakia	2800	280
France	7000	127
Germany	31800	418
Greece	1628	155
Hungary	1232	112
Ireland	15	4
Israel	300	60
Italy	4100	72
The Netherlands	4236	277
Norway	1020	255
Portugal	682	68
Slovenia	515	258
Spain	7000	200
Sweden	3982	442
Switzerland	1607	268
Turkey	1240	21
United Kingdom	11435	204
Total	82892	191

Table 5. Indications for radionuclide therapy in 15 European countries[a]

Country	Benign thyroid disease	Arthritic diseases	Malignant diseases
Austria	1400 (10)	20 (4)	217 (13.3%)
Czech Republic + Slovakia	550 (6)	242 (6)	1011 (56.1%)
Germany	22890 (115)	1388 (51)	7524 (23.7%)
Greece	850 (n.a.)	115 (n.a.)	663 (40.7%)
Hungary	1023 (10)	20 (4)	79 (7.0%)
Ireland	n.a.	4 (1)	20
Israel	n.a.	1 (1)	6
Italy	1400 (55)	–	2800 (66.7%)
The Netherlands	3318 (27)	369 (20)	976 (20.9%)
Norway	796 (21)	4 (1)	220 (21.6%)
Portugal	295 (4)	4 (1)	383 (56.2%)
Slovenia	393 (5)	32 (1)	90 (17.5%)
Switzerland	896 (23)	188 (11)	261 (19.4%)
Turkey	750 (11)	–	490 (39.5%)
United Kingdom	9059 (88)	321 (37)	2055 (18.0%)
Total	43620 (69.1%)	2708 (4.3%)	16795 (26.6%)

[a] The number of centres performing a particular type of therapy are added in parentheses in the first two columns. In the last column, treatments for oncological indications are given as a percentage of all therapies

Number of patients treated

Data on the number of patients undergoing radionuclide therapy are available for 18 European countries. The total number of patients treated in these countries was 82892, i.e. a prevalence of 191 patients treated per 1 million inhabitants. Table 4 breaks this number down into the absolute number of patients treated and their relative prevalence in individual countries. It becomes clear that in countries with a low density of isolation facilities the prevalence of treated patients remains low as well.

Indications

Complete information about the indications for radionuclide therapy was obtained from 15 countries. Table 5 divides the indications into benign (thyroid and arthritic disease) and malignant diseases.

The majority of treatments (69.1%) are undertaken for benign thyroid disease; arthritic disease at present accounts for only 4.3% of indications, which suggests an underutilisation of this form of treatment in most countries.

The overall percentage of malignant diseases as an indication for radionuclide therapy, which generally require a greater amount of radioactivity to be administered and more stringent isolation of patients, is 26.6%, although the relative incidence varies considerably between countries (7.0%–66.7%).

Table 6 lists the types of oncological indications: the great majority of treatments in this group are accounted

Table 6. Oncological indications for radionuclide therapy in 16 European countries

Country	Thyroid ca. (^{131}I therapy)	Haematology (^{32}P therapy)	Bone palliation (bone therapy)	Neural crest tumours (^{131}I MIBG)	Other indications[b, c]
Austria	145 (8)	5 (3)	60 (6)	2 (1)	5 (3)
Czech Republic + Slovakia	700 (5)	7 (2)	300 (6)	4 (2)	–
France	n.a.	n.a.	500 (60)	n.a.	n.a.
Germany	6388 (79)	150 (46)	717 (45)	n.a. (6)	269[b] (26)
Greece	489 (n.a.)	–	174 (n.a.)	–	–
Hungary	61 (1)	–	10 (4)	8 (1)	–
Ireland	20 (2)	– (4)	– (4)	– (1)	–
Israel	4 (7)	–	1 (1)	1 (3)	–
Italy	1800 (31)	–	700 (30)	200 (5)	100[c] (2)
The Netherlands	484 (16)	91 (16)	296 (24)	92 (7)	13[b] (6)
Norway	145 (8)	3 (1)	63 (7)	3 (1)	6 (1)
Portugal	349 (4)	5 (2)	26 (3)	3 (2)	–
Slovenia	67 (1)	–	19 (3)	2 (1)	2 (1)
Switzerland	165 (8)	10 (5)	77 (10)	5 (2)	4 (2)
Turkey	470 (7)	5 (3)	15 (2)	–	–
United Kingdom	911 (50)	569 (59)	425 (49)	76 (11)	56[b] (12)
Total	12198	845	3383	396	455

n.a., Not available

[a] The number of centres performing a particular type of therapy is given in parentheses

[b,c] Other indications include: [b] intracavitary therapy and [c] direct intratumoral administration

Table 7. Cumulative amounts of radioactivities in GBq, administered for radionuclide therapy in 13 European countries

Country	^{131}I	^{90}Y	^{186}Re colloid	^{32}P	^{131}I- MIBG	^{89}Sr	^{186}Re-HEDP	Others
Austria	3500	10	–	0.2	3.3	7.5	15	37
Czech Republic + Slovakia	4000	55	12	15	12	15	–	8
Germany	41426	1025	113	23	477	13	229	95[a]
Hungary	951	9.3	–	–	24.9	1.5	–	–
Israel	1000	740	–	–	7.4	–	37	–
The Netherlands	2900	75	2	18	510	42	60	–
Norway	932	1.9	–	0.33	11.1	9.4	–	9
Portugal	1194	0.74	–	1.66	18.5	3	–	–
Slovenia	582	7.59	–	1.3	15	2	–	–
Spain	10000	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Switzerland	1690	31	n.a.	11	1	8	12	–
Turkey	2080	–	–	0.45	14.8	2.22	–	–
United Kingdom	16695	88	–	94.96	646	57.06	16	191
Total	86950	2043.5	127	165.9	1741	160.68	369	340

n.a., Not available
[a] ^{169}Er colloid

for by patients receiving high-dose ^{131}I therapy for differentiated thyroid carcinoma. Therapy with bone-seeking agents for palliation of skeletal metastases is the second most common oncological indication, but other, less frequent indications, such as phosphorus-32 therapy for haematological disorders, ^{131}I MIBG therapy for neural crest tumours, radioimmunotherapy, and intracavitary and intratumoral applications are growing and will certainly become more prominent in the (very) near future.

Administered activities

Complete information on the cumulatively administered quantities of the various therapeutic radiopharmaceuticals is available for only 13 European countries. The overall total is 91897 GBq, the majority of which is in the form of ^{131}I.

Table 7 shows the cumulative data for individual countries. As most of this activity administered to patients will be excreted relatively rapidly, it is fair to assume that these figures approach the total quantity of radioactive waste to be stored.

Conclusions

It is concluded that a wide variation in therapy practice exists across Europe, particularly in the utilisation of radionuclide therapy, the requirement and availability of proper isolation facilities and the background training of those undertaking therapy. More uniform guidelines and legislation are required, although changes in legislation may have a significant impact in some countries. Although there is wide variation in the therapies used in each country, on the whole it appears that there is an underutilisation of nuclear medicine as a therapeutic modality. A rapidly increasing role may be expected, in particular for oncological indications requiring high-dose radionuclide treatment. Therefore there is an urgent need for a greater number of isolation beds in dedicated centres throughout Europe. An insufficient number of isolation beds and limited resources will delay the implementation of current and newly developed forms of radionuclide treatment in many countries.

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