MRT and dosimetry: The EANM perspective

Rationale for dosimetry

Patient protection

Treatment optimisation

Standardisation

Regulatory requirements

Rationale for dosimetry

Patient protection

Treatment optimisation

Standardisation

Regulatory requirements

Secondary malignancies – mIBG therapy

The Turkish Journal of Pediatrics 2011; 53: 83-86 *Case*

Secondary childhood acute myeloid leukemia with complex karyotypic anomalies including monosomy 7, monosomy 5 and translocation (1;10) after ^{131}I- metaiodobenzylguanidine therapy for relapsed neuroblastoma

Sonay İncesoy-Özdemir[1], Ceyhun Bozkurt[1], Nazmiye Yüksek[1], Ayşe Ceyda Ören[1], Gürses Şahin[1], Süreyya Bozkurt[2], Ulya Ertem[1]

[1]Department of Pediatric Oncology, Dr. Sami Ulus Children's Hospital, and [2]Department of Basic Oncology, Hacettepe University Institute of Oncology, Ankara, Turkey

SUMMARY: İncesoy-Özdemir S, Bozkurt C, Yüksek N, Ören AC, Şahin G, Bozkurt S, Ertem U. Secondary childhood acute myeloid leukemia with complex karyotypic anomalies including monosomy 7, monosomy 5 and translocation (1;10) after ^{131}I-metaiodobenzylguanidine therapy for relapsed neuroblastoma. Turk J Pediatr 2011; 53: 83-86.

The prognosis for relapsing or refractory neuroblastoma (NB) remains dismal, with a five-year disease-free survival of <20%, and no effective salvage treatment has been identified so far. ^{131}I-metaiodobenzylguanidine (^{131}I-MIBG) has come to play an essential role in the imaging and therapy of NB over the past 30 years. The role of ^{131}I-MIBG in the treatment of NB is continually expanding. ^{131}I-MIBG treatment together with cumulative doses of other alkylating agents has potential serious late side effects such as myelodysplasia and leukemia, although rare. We describe a secondary acute myeloid leukemia case with complex karyotypic anomalies that included monosomy 5, monosomy 7 and translocation (1;10) in a child with relapsed NB who received therapeutic ^{131}I-MIBG.

Key words: ^{131}I-metaiodobenzylguanidine, monosomy 5 and 7, neuroblastoma, secondary myeloid leukemia, translocation (1;10).

Secondary malignancies – mIBG therapy

The Turkish Journal of Pediatrics 2011; 53: 83-86 *Case*

Secondary childhood acute myeloid leukemia with complex karyotypic anomalies including monosomy 7, monosomy 5 and translocation (1;10) after ^{131}I- metaiodobenzylguanidine therap

Sonay İn
Gürses Ş
[1]Department
University In

Original Article

Secondary Myelodysplastic Syndrome and Leukemia Following ^{131}I-Metaiodobenzylguanidine Therapy for Relapsed Neuroblastoma

Brian Weiss, MD, Amish Vora, MD, John Huberty, MSc,
Randall A. Hawkins, MD, PhD, and Katherine K. Matthay, MD

Purpose: To describe three patients with secondary leukemia after treatment with ^{131}I-metaiodobenzylguanidine (MIBG) for neuroblastoma.
Methods: Of 95 children with refractory neuroblastoma treated with ^{131}I-MIBG at UCSF, 3 have been identified with secondary myelodysplasia/leukemia. The case records and bone marrow results were reviewed, along with a review of the literature.
Results: Three patients developed secondary myelodysplasia/leukemia, at 7, 11, and 12 months following ^{131}I-MIBG therapy. Cytogenetic abnormalities included –7q/–5, –7/+2q37, –11 and +12. Three additional cases were found in literature review of 509 reported patients treated with ^{131}I-MIBG for neuroblastoma.
Conclusions: Therapy with ^{131}I-MIBG may contribute to the risk of secondary leukemia in patients who have received intensive chemotherapy, thought the risk of this complication is far lower than the risk of disease progression. Further monitoring for this complication is indicated.
Key Words: acute myelogenous leukemia, ^{131}I-MIBG, myelodysplasia, neuroblastoma, secondary leukemia

shown to concentrate in neuroblastoma and therefore holds promise for cell-specific radiation treatment of this tumor. Multiple trials of ^{131}I-MIBG have shown significant response rates of 30% to 40% and apparent prolongation of survival in children treated after relapse.[2,3] More recently, some centers have begun testing the use of this agent in newly diagnosed patients and have shown good response rates and minimal toxicity.[4]

The intensity of therapy required to successfully treat neuroblastoma necessitates careful consideration of the possible serious late sequelae. Others have reported that increased dose intensity of alkylating agents and etoposide results in a significant percentage of children treated for neuroblastoma developing second malignant neoplasm (SMN), particularly myelodysplasia (MDS) and leukemia.[5] Alkylating agents, topoisomerase inhibitors, and irradiation are all currently important components of induction and myeloablative protocols for neuroblastoma, and all may increase the risk of SMN in long-term survivors. In the ex-

Secondary malignancies – mIBG therapy

The Turkish Journal of Pediatrics 2011; 53: 83-86 Case

Secondary childhood acute myeloid leukemia with complex karyotypic anomalies including monosomy 7, monosomy 5 and translocation (1;10) after ^{131}I- metaiodobenzylguanidine therap

Sonay İn
Gürses Ş
[1]Department
University In

Original Article

Secondary Myelodysplastic Syndrome and Leukemia Following ^{131}I-Metaiodobenzylguanidine Therapy for Relapsed Neuroblastoma

Brian Weiss, MD, Amish Vora, MD, John Huberty, MSc,
Ra

3 patients of 95 developed secondary malignancies

'The risk is lower than that of disease progression'

Pur
trea
bla
Me
wit
my
sult
Res
sia/
ther
–11 and +12. Three additional cases were found in literature re-
view of 509 reported patients treated with ^{131}I-MIBG for neuroblastoma.

Conclusions: Therapy with ^{131}I-MIBG may contribute to the risk of secondary leukemia in patients who have received intensive chemotherapy, thought the risk of this complication is far lower than the risk of disease progression. Further monitoring for this complication is indicated.

Key Words: acute myelogenous leukemia, ^{131}I-MIBG, myelodysplasia, neuroblastoma, secondary leukemia

sible serious late sequelae. Others have reported that increased dose intensity of alkylating agents and etoposide results in a significant percentage of children treated for neuroblastoma developing second malignant neoplasm (SMN), particularly myelodysplasia (MDS) and leukemia.[5] Alkylating agents, topoisomerase inhibitors, and irradiation are all currently important components of induction and myeloablative protocols for neuroblastoma, and all may increase the risk of SMN in long-term survivors. In the ex-

Secondary malignancies – mIBG therapy

The Turkish Journal of Pediatrics 2011; 53: 83-86 *Case*

Secondary childhood acute myeloid leukemia with complex karyotypic anomalies including monosomy 7, monosomy 5 and translocation (1;10) after ^{131}I- metaiodobenzylguanidine therap

Sonay İn
Gürses Ş
[1]Department
University In

Original Article

Secondary Myelodysplastic Syndrome and Leukemia Following ^{131}I-Metaiodobenzylguanidine Therapy for Relapsed Neuroblastoma

Brian Weiss, MD, Amish Vora, MD, John Huberty, MSc,
Randall A. Hawkins, MD, PhD, and Katherine K. Matthay, MD

Purpose: To describe three patients with secondary leu
treatment with ^{131}I-metaiodobenzylguanidine (MIBG)
blastoma.
Methods: Of 95 children with refractory neuroblasto
with ^{131}I-MIBG at UCSF, 3 have been identified with
myelodysplasia/leukemia. The case records and bone
sults were reviewed, along with a review of the literat
Results: Three patients developed secondary my
sia/leukemia, at 7, 11, and 12 months following
therapy. Cytogenetic abnormalities included –7q/–5,
–11 and +12. Three additional cases were found in li
view of 509 reported patients treated with ^{131}I-MIBG
blastoma.
Conclusions: Therapy with ^{131}I-MIBG may contribute
of secondary leukemia in patients who have receive
chemotherapy, thought the risk of this complication i
than the risk of disease progression. Further monitor
complication is indicated.
Key Words: acute myelogenous leukemia, ^{131}I-MIBG
plasia, neuroblastoma, secondary leukemia

Cancer. 2003 Mar 1;97(5):1332-8.

Second malignancies in children with neuroblastoma after combined treatment with 131I-metaiodobenzylguanidine.

Garaventa A[1], Gambini C, Villavecchia G, Di Cataldo A, Bertolazzi L, Pizzitola MR, De Bernardi B, Haupt R.

Author information

Abstract

BACKGROUND: (131)I-metaiodobenzylguanidine ((131)I-MIBG) is selectively taken up by cells of neural crest origin, allowing targeted radiotherapy of tumors such as neuroblastoma (NB) and pheochromocytoma. Radiotherapy may provide additional benefits in the treatment of NB, with moderate side effects such as hematologic and thyroid toxicity. However, with longer follow-up, other complications might occur. We describe our experience with second cancers occurring in children treated with (131)I-MIBG and chemotherapy.

METHODS: The clinical records of 119 consecutive NB cases treated with (131)I-MIBG at a single institution between 1984 and 2001 were reviewed for the occurrence of a second malignant neoplasm (SMN).

RESULTS: Overall, five cases of SMN occurred in the study patients. In particular, two cases of myeloid leukemia, one of angiomatous fibrous histiocytoma, one of malignant schwannoma, and one case of rhabdomyosarcoma were detected. The schwannoma and the rhabdomyosarcoma developed within the residual neuroblastic mass after first-line therapy.

CONCLUSIONS: Should (131)I-MIBG treatment become more broadly employed in the therapeutic strategy for neuroblastoma, the risk of second cancer will have to be taken into consideration. The organization of an international registry of subjects treated with (131)I-MIBG might better define the frequency and features of second malignancies following this radiometabolic approach.

Secondary malignancies – mIBG therapy

The Turkish Journal of Pediatrics 2011; 53: 83-86 *Case*

Secondary childhood acute myeloid leukemia with complex karyotypic anomalies including monosomy 7, monosomy 5 and translocation (1;10) after ^{131}I- metaiodobenzylguanidine therap

Sonay İn
Gürses Ş
[1]Department
University In

Original Article

Secondary Myelodysplastic Syndrome and Leukemia Following ^{131}I-Metaiodobenzylguanidine Therapy for Relapsed Neuroblastoma

Brian Weiss, MD, Amish Vora, MD, John Huberty, MSc,
Randall A. Hawkins, MD, PhD, and Katherine K. Matthay, MD

Purpose: To describe three patients with secondary leu
treatment with ^{131}I-metaiodobenzylguanidine (MIBG)
blastoma.
Methods: Of 95 children with refractory neuroblasto
with ^{131}I-MIBG at UCSF, 3 have been identified with
myelodysplasia/leukemia. The case records and bone
sults were reviewed, along with a review of the literat
Results: Three patients developed secondary my
sia/leukemia, at 7, 11, and 12 months following
therapy. Cytogenetic abnormalities included –7q/–5,
–11 and +12. Three additional cases were found in li
view of 509 reported patients treated with ^{131}I-MIBG
blastoma.
Conclusions: Therapy with ^{131}I-MIBG may contribute
of secondary leukemia in patients who have receive
chemotherapy, thought the risk of this complication i
than the risk of disease progression. Further monitor
complication is indicated.
Key Words: acute myelogenous leukemia, ^{131}I-MIBG
plasia, neuroblastoma, secondary leukemia

Cancer. 2003 Mar 1;97(5):1332-8.

Second malignancies in children with neuroblastoma after combined treatment with 131I-metaiodobenzylguanidine.

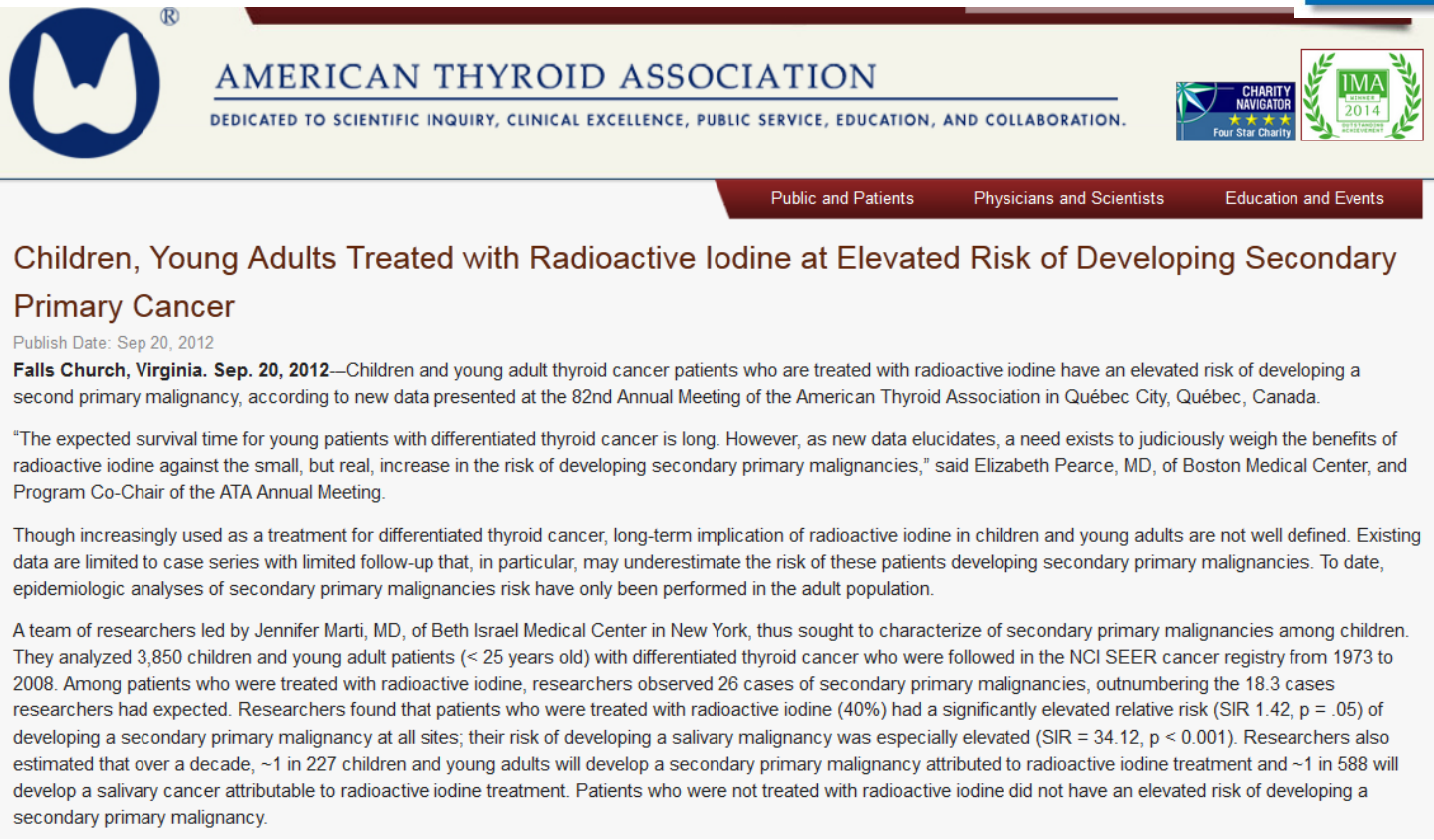
Garaventa A[1], Gambini C, Villavecchia G, Di Cataldo A, Bertolazzi L, Pizzitola MR, De Bernardi B, Haupt R.

Author information

Abs
BAC
radi
NB,
desc
MET
revie
RES
histi
rhab
CONCLUSIONS: Should (131)I-MIBG treatment become more broadly employed in the therapeutic strategy for neuroblastoma, the risk of second cancer will have to be taken into consideration. The organization of an international registry of subjects treated with (131)I-MIBG might better define the frequency and features of second malignancies following this radiometabolic approach.

5 patients of 119 developed secondary malignancies

An international registry is needed…



AMERICAN THYROID ASSOCIATION

DEDICATED TO SCIENTIFIC INQUIRY, CLINICAL EXCELLENCE, PUBLIC SERVICE, EDUCATION, AND COLLABORATION.

CHARITY NAVIGATOR Four Star Charity

IMA 2014

Public and Patients | Physicians and Scientists | Education and Events

Children, Young Adults Treated with Radioactive Iodine at Elevated Risk of Developing Secondary Primary Cancer

Publish Date: Sep 20, 2012

Falls Church, Virginia. Sep. 20, 2012—Children and young adult thyroid cancer patients who are treated with radioactive iodine have an elevated risk of developing a second primary malignancy, according to new data presented at the 82nd Annual Meeting of the American Thyroid Association in Québec City, Québec, Canada.

"The expected survival time for young patients with differentiated thyroid cancer is long. However, as new data elucidates, a need exists to judiciously weigh the benefits of radioactive iodine against the small, but real, increase in the risk of developing secondary primary malignancies," said Elizabeth Pearce, MD, of Boston Medical Center, and Program Co-Chair of the ATA Annual Meeting.

Though increasingly used as a treatment for differentiated thyroid cancer, long-term implication of radioactive iodine in children and young adults are not well defined. Existing data are limited to case series with limited follow-up that, in particular, may underestimate the risk of these patients developing secondary primary malignancies. To date, epidemiologic analyses of secondary primary malignancies risk have only been performed in the adult population.

A team of researchers led by Jennifer Marti, MD, of Beth Israel Medical Center in New York, thus sought to characterize of secondary primary malignancies among children. They analyzed 3,850 children and young adult patients (< 25 years old) with differentiated thyroid cancer who were followed in the NCI SEER cancer registry from 1973 to 2008. Among patients who were treated with radioactive iodine, researchers observed 26 cases of secondary primary malignancies, outnumbering the 18.3 cases researchers had expected. Researchers found that patients who were treated with radioactive iodine (40%) had a significantly elevated relative risk (SIR 1.42, $p = .05$) of developing a secondary primary malignancy at all sites; their risk of developing a salivary malignancy was especially elevated (SIR = 34.12, $p < 0.001$). Researchers also estimated that over a decade, ~1 in 227 children and young adults will develop a secondary primary malignancy attributed to radioactive iodine treatment and ~1 in 588 will develop a salivary cancer attributable to radioactive iodine treatment. Patients who were not treated with radioactive iodine did not have an elevated risk of developing a secondary primary malignancy.

1 in 227 children treated with radioiodine will develop a secondary primary malignancy

Eur J Nucl Med Mol Imaging (2014) 41:1976–1988
DOI 10.1007/s00259-014-2824-5

REVIEW ARTICLE

The evidence base for the use of internal dosimetry in the clinical practice of molecular radiotherapy

Lidia Strigari · Mark Konijnenberg · Carlo Chiesa · Manuel Bardies · Yong Du · Katarina Sjögreen Gleisner · Michael Lassmann · Glenn Flux

Received: 15 May 2014 / Accepted: 19 May 2014 / Published online: 11 June 2014

Abstract Molecular radiotherapy (MRT) has demonstrated unique therapeutic advantages in the treatment of an increasing number of cancers. As with other treatment modalities, there is related toxicity to a number of organs at risk. Despite the large number of clinical trials over the past several de- 79 studies investigating dosimetry, an absorbed dose–effect correlation was found in 48. The application of radiobiological modelling to clinical data is of increasing importance and the limited published data on absorbed dose–effect relationships based on these models are also reviewed. Based on

Patient protection

Benua *et al* – 1-2 Gy blood absorbed dose gave severe radiation complication in 1 of 24 cases, 2-3 Gy gave severe complications in 5 of 33 cases, 1 fatal.

Buckley *et al*, Matthay *et al* found correlations of dose with neutropenia and thrombocytopenia

Barone *et al* found ADER in renal failure with Y-90 DOTATOC

Mones *et al*, Ferrer *et al* found ADER (haematological toxicity) for Bexxar & Zevalin

Sangro *et al* found 20% toxicity in patients treated with 37 Gy with microspheres, compared to 26 Gy for no toxicity

Buffa *et al* - correlation between dose and WBC and platelet toxicity

Patient protection

Potential for further radiation therapy. Is previous MRT dose important?

Complications determined by clinical factors as well as AD, including previous treatments

Need to determine 'acceptable toxicity'?

Patients undergoing radionuclide therapy are the only population that do not have radiation doses calculated

Potential for centres to be sued

No toxicity seen in some patients – more aggressive treatment is warranted

Rationale for dosimetry

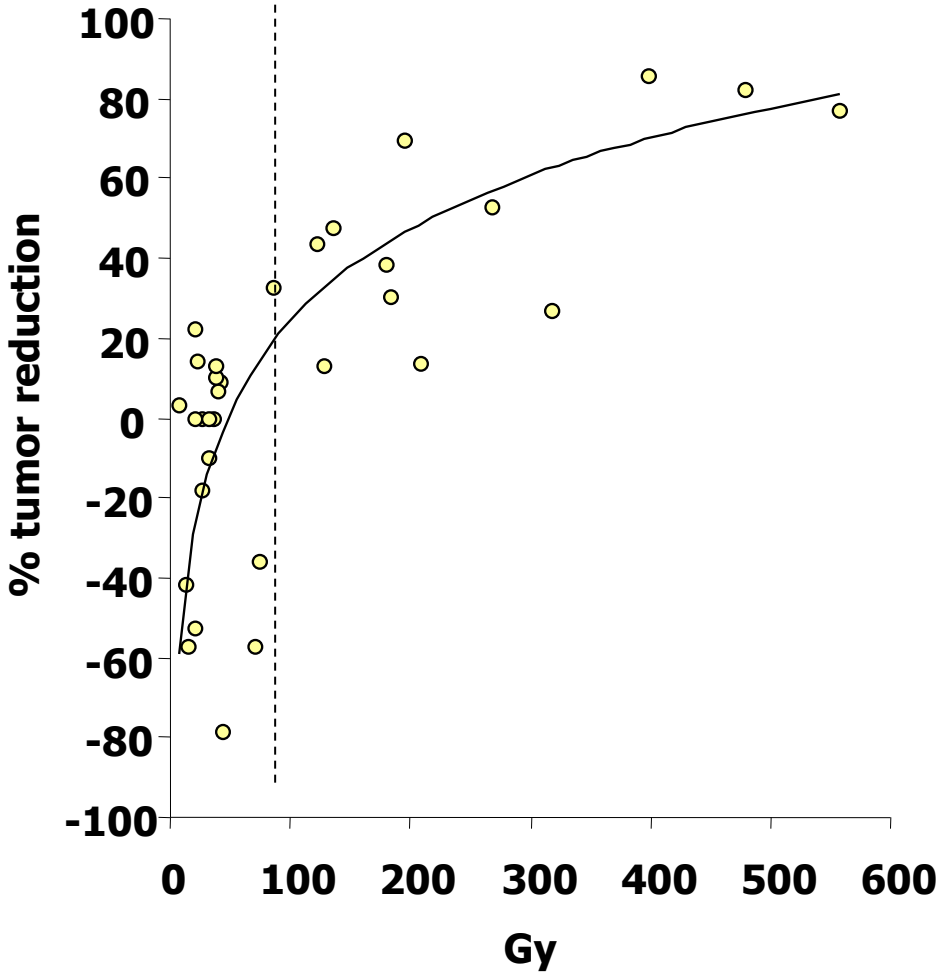
Patient protection

Treatment optimisation

Standardisation

Regulatory requirements

Correlation tumor response vs dose (measured with PET and CT-scan) at end of treatment ^{90}Y-SMT-487 trial (n = 32)



Stephan Walrand - UCL Brussels

Radioiodine for thyroid cancer

Table 4 Studies showing dose–effect relationships for ^{131}I (NaI) therapy against DTC

Reference	No. of patients	Endpoint	Threshold dose
[13]	50	Ablation	300 Gy (remnant)
[13]	26	Response	80 Gy (metastases)
[14]	23	Ablation	49 Gy (remnant)
[15]	449	Ablation	0.35 Gy (blood)
[16]	122	Complications	2 Gy (blood)
[17]	198	Toxicity grade 3 or more	2 Gy (blood)
[18]	17	Toxicity grade 3 or more	1.7 Gy (blood)

Strigari *et al EJNMMI 2014*

Radioiodine for thyroid cancer

Table 4 Studies showing dose–effect relationships for ^{131}I (NaI) therapy against DTC

Reference	No. of patients	Endpoint	Threshold dose
[13]	50	Ablation	300 Gy (remnant)
[13]	26	R	
[14]	23	A	
[15]	449	A	
[16]	122	C	
[17]	198	T	
[18]	17	T	

Table 5 Studies showing dose–effect relationships for control of benign thyroid disease with ^{131}I (NaI) in Graves' disease

Reference	No. of patients	Endpoint	Efficacy threshold (thyroid)
[19]	92	>60 % size reduction	200 Gy
[20]	205	80 % cure hyperthyroidism	200 Gy
[23]	79	50 % hypothyroidism	60 Gy (96 Gy multinodular disease)
[26]	147	Hypothyroidism	400 Gy

Strigari *et al EJNMMI 2014*

Dose – effect for NHL and microsphere treatments

Eur J Nucl Med Mol Imaging (2014) 41:1976–1988

Reference	No. of patients	Endpoint	Threshold dose
[37]	76	OS	0.75 Gy (WB)
[39]	20	PR (>50 % shrinkage)	2 Gy effective uniform dose (tumour)
[40]	10	PR (>80 % shrinkage)	4.5 Gy (tumour), p=0.06
[42]	37	PFS	20 Gy (WB)
[43]	19	Cardiopulmonary toxicity	25 Gy (WB)
[44]	14	Reversible BM toxicity	0.45 Gy (WB)

Strigari *et al EJNMMI 2014*

Dose – effect for NHL and microsphere treatments

Reference	No. of patients	Endpoint	Threshold dose
[37]	76	OS	0.75 Gy (WB)
[39]	20	PR (>50 % shrinkage)	2 Gy effective uniform dose (tumour)
[40]	10		
[42]	37		
[43]	19		
[44]	14		

Table 9 Studies showing dose–effect relationships for intraarterial therapy of liver cancer using radiolabelled microspheres

Reference	No. of patients	Radionuclide	Carrier	Endpoint	Threshold dose
[47]	71	^{90}Y	Ivalon microspheres	PR (>50 % reduction), pneumonitis	225 Gy (lesion), 30/50 Gy (lung)
[48]	36	^{90}Y	Glass microspheres	Response (PR+CR)	205 Gy (lesion)
[49]	185	^{188}Re	Lipiodol	OS	30 Gy (tumour)
[50]	12	^{90}Y	Resin microspheres	Metabolic FDG response>50 %	260 Gy (tumour)
[51]	8	^{90}Y	Resin microspheres	Metabolic FDG response >50 %	46 Gy (tumour)
[52]	52	^{90}Y	Glass microspheres	EASL density response (PR+CR)	500 Gy (lesion)
[53]	73	^{90}Y	Resin microspheres	50% TCP (PR+CR) 5 %≥G2 liver toxicity	150 Gy (tumour), 50 Gy BED (liver)
[54]	45	^{90}Y	Resin microspheres	REILD	40 Gy (liver)
[55]	52	^{90}Y	Glass microspheres	Tumour density reduction, liver decompensation	200 Gy (tumour), >60 Gy to the parenchyma
[56]	15	^{166}Ho	Polylactic acid microspheres	G3 liver and blood toxicity	80 Gy (liver)

Strigari *et al EJNMMI 2014*

Dose – effect for NHL and microsphere treatments

Reference	No. of patients	Endpoint	Threshold dose
[37]	76	OS	0.75 Gy (WB)
[39]	20	PR (>50 % shrinkage)	2 Gy effective uniform dose (tumour)
[40]	10		
[42]	37		
[43]	19		
[44]	14		

Table 9 Studies showing dose–effect relationships for intraarterial therapy of liver cancer using radiolabelled microspheres

Reference	No. of patients	Radionuclide	Carrier	Endpoint	Threshold dose
[47]	71	^{90}Y	Ivalon microspheres	PR (>50 % reduction), pneumonitis	225 Gy (lesion), 30/50 Gy (lung)
[48]	36	^{90}Y	Glass microspheres	Response (PR+CR)	205 Gy (lesion)
[49]	185	^{188}Re	Lipiodol	OS	30 Gy (tumour)
[50]	12	^{90}Y	Resin microspheres	Metabolic FDG response>50 %	260 Gy (tumour)
[51]	8	^{90}Y	Resin microspheres	Metabolic FDG response >50 %	46 Gy (tumour)
[52]	52	^{90}Y	Glass microspheres	EASL density response (PR+CR)	500 Gy (lesion)
[53]	73	^{90}Y	Resin microspheres	50% TCP (PR+CR) 5 %≥G2 liver toxicity	150 Gy (tumour), 50 Gy BED (liver)
[54]	45	^{90}Y	Resin microspheres	REILD	40 Gy (liver)
[55]	52	^{90}Y	Glass microspheres	Tumour density reduction, liver decompensation	200 Gy (tumour), >60 Gy to the parenchyma
[56]	15	^{166}Ho	Polylactic acid microspheres	G3 liver and blood toxicity	80 Gy (liver)

Correlations also found for I-131 mIBG of neuroblastoma (Matthay *et al*) and lymphoma (Kaminski, Wahl, Ferrer…)

Strigari *et al EJNMMI 2014*

Rationale for dosimetry

Patient protection

Treatment optimisation

Standardisation

Regulatory requirements

Industry led standardisation

Sr-89 for bone metastases: 150 MBq

Sm-153 for bone metastases: 37kBq/kg

Ra-223 for bone metastases: 50 kBq/kg for 6 treatments

Zevalin for NHL: 14.8 MBq/kg for patients with normal platelets, 11.1 MBq/kg if relapsed or refractory, maximum 1184 MBq

Bexxar for NHL: 75 cGy WB dose

Y-90 microspheres for HCC and liver metastases: Various models for glass and resin microspheres

Radioiodine for ca & benign thyroid

EANM Guidelines: 'The "optimal" activity for radioiodine ablation of post-surgical thyroid residues macroscopic disease is generally a single administration of 1 - 5 GBq.

For radioiodine ablation in children, some centres adjust activity by body weight (e.g. to 1.85–7.4 MBq/kg) or surface area or by age.'

Guidelines for radioiodine therapy of differentiated thyroid cancer

M. Luster · S. E. Clarke · M. Dietlein · M. Lassmann · P. Lind · W. J. G. Oyen · J. Tennvall · E. Bombardieri

ATA: 'No prospective randomized trial to address the optimal therapeutic approach has been published.' The RAI activity administered can be given empirically or determined by dosimetry.

FDA: For thyroid carcinoma, the usual sodium iodide I-131 therapeutic dose is 3700 to 5550 MBq. For ablation of post-operative residual thyroid tissue, the usual dose is 1850 MBq.

Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer

David S. Cooper, M.D.[1] (Chair)*, Gerard M. Doherty, M.D.,[2] Bryan R. Haugen, M.D.,[3] Richard T. Kloos, M.D.,[4] Stephanie L. Lee, M.D., Ph.D.,[5] Susan J. Mandel, M.D., M.P.H.,[6] Ernest L. Mazzaferri, M.D.,[7] Bryan McIver, M.D., Ph.D.,[8] Furio Pacini, M.D.,[9] Martin Schlumberger, M.D.,[10] Steven I. Sherman, M.D.,[11] David L. Steward, M.D.,[12] and R. Michael Tuttle, M.D.[13]

EANM guidelines

Dosimetry Committee Publications

1. Hesse B, Tagil K, Cuocolo A, Anagnostopoulos C, Bardies M, Bax J, et al. EANM/ESC procedural guidelines for myocardial perfusion imaging in nuclear cardiology. Eur J Nucl Med Mol Imaging. 2005;32:855-97.
2. Flux G, Bardies M, Monsieurs M, Savolainen S, Strands SE, Lassmann M, et al. The impact of PET and SPECT on dosimetry for targeted radionuclide therapy. Zeitschrift fur medizinische Physik. 2006;16:47-59.
3. Tennvall J, Brans B. EANM procedure guideline for 32P phosphate treatment of myeloproliferative diseases. Eur J Nucl Med Mol Imaging. 2007;34:1324-7.
4. Tennvall J, Fischer M, Bischof Delaloye A, Bombardieri E, Bodei L, Giammarile F, et al. EANM procedure guideline for radio-immunotherapy for B-cell lymphoma with 90Y-radiolabelled ibritumomab tiuxetan (Zevalin). Eur J Nucl Med Mol Imaging. 2007;34:616-22.
5. Bodei L, Lam M, Chiesa C, Flux G, Brans B, Chiti A, et al. EANM procedure guideline for treatment of refractory metastatic bone pain. Eur J Nucl Med Mol Imaging. 2008;35:1934-40.
6. Giammarile F, Chiti A, Lassmann M, Brans B, Flux G, Eanm. EANM procedure guidelines for 131I-meta-iodobenzylguanidine (131I-mIBG) therapy. Eur J Nucl Med Mol Imaging. 2008;35:1039-47.
7. Lassmann M, Biassoni L, Monsieurs M, Franzius C, Dosimetry E, Paediatrics C. The new EANM paediatric dosage card: additional notes with respect to F-18. Eur J Nucl Med Mol Imaging. 2008;35:1666-8.
8. Lassmann M, Biassoni L, Monsieurs M, Franzius C, Jacobs F, Dosimetry E, et al. The new EANM paediatric dosage card. Eur J Nucl Med Mol Imaging. 2008;35:1748.
9. Lassmann M, Hanscheid H, Chiesa C, Hindorf C, Flux G, Luster M, et al. EANM Dosimetry Committee series on standard operational procedures for pre-therapeutic dosimetry I: blood and bone marrow dosimetry in differentiated thyroid cancer therapy. Eur J Nucl Med Mol Imaging. 2008;35:1405-12.
10. Hindorf C, Glatting G, Chiesa C, Linden O, Flux G. EANM Dosimetry Committee guidelines for bone marrow and whole-body dosimetry. Eur J Nucl Med Mol Imaging. 2010;37:1238-50.
11. Stokkel MP, Handkiewicz Junak D, Lassmann M, Dietlein M, Luster M. EANM procedure guidelines for therapy of benign thyroid disease. Eur J Nucl Med Mol Imaging. 2010;37:2218-28.
12. Giammarile F, Bodei L, Chiesa C, Flux G, Forrer F, Kraeber-Bodere F, et al. EANM procedure guideline for the treatment of liver cancer and liver metastases with intra-arterial radioactive compounds. Eur J Nucl Med Mol Imaging. 2011;38:1393-406.
13. Lassmann M, Chiesa C, Flux G, Bardies M. EANM Dosimetry Committee guidance document: good practice of clinical dosimetry reporting. Eur J Nucl Med Mol Imaging. 2011;38:192-200.
14. Del Guerra A, Bardies M, Belcari N, Caruana CJ, Christofides S, Erba P, et al. Curriculum for education and training of medical physicists in nuclear medicine: recommendations from the EANM Physics Committee, the EANM Dosimetry Committee and EFOMP. Physica medica 2013;29:139-62.
15. Hanscheid H, Canzi C, Eschner W, Flux G, Luster M, Strigari L, et al. EANM Dosimetry Committee Series on Standard Operational Procedures for Pre-Therapeutic Dosimetry II Dosimetry prior to radioiodine therapy of benign thyroid diseases. Eur J Nucl Med Mol Imaging. 2013.
16. Lonsdale MN, Bardies M, Boellaard R, Christofides S, Flux G, Lassmann M, et al. EFOMP and EANM: joint recommendations for a curriculum for the education and training of physicists in nuclear medicine. Eur J Nucl Med Mol Imaging. 2013;40:645-8.
17. Lonsdale MN, Lassmann M. EANM perspective. Radiat Prot Dosimetry. 2013;153:166-9

EANM Standardisation for dosimetry

GUIDELINES

EANM Dosimetry Committee series on standard operational procedures for pre-therapeutic dosimetry I: blood and bone marrow dosimetry in differentiated thyroid cancer therapy

Michael Lassmann · Heribert Hänscheid · Carlo Chiesa · Cecilia Hindorf · Glenn Flux · Markus Luster

Abstract
Introduction The purpose of the EANM Dosimetry Committee Series on "Standard Operational Procedures for Pre-therapeutic Dosimetry" (SOP) is to provide advice to scientists and clinicians on how to perform pre-therapeutic and/or therapeutic patient-specific absorbed dose assessments.
Material and Methods This particular SOP gives advice on how to tailor the therapeutic activity to be administered for systemic treatment of differentiated thyroid cancer (DTC) such that the absorbed dose to the blood does not exceed 2 Gy (a widely accepted limit for bone marrow toxicity). The methodology of blood-based dosimetry has been developed in the 1960s and refined in a series of international multi-centre trials in the framework of the introduction of new diagnostic and therapeutic tools, e.g. recombinant human thyroid-stimulating hormone in the management of DTC.
Conclusion The intention is to guide the user through a series of measurements and calculations which the authors consider to be the best and most reproducible way at present.

Keywords Dosimetry · Thyroid cancer · SOP

Introduction

The purpose of this EANM Dosimetry Committee Series on

EANM Standardisation for dosimetry

Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-013-2387-x

GUIDELINES

EANM Dosimetry Committee Series on Standard Operational Procedures for Pre-Therapeutic Dosimetry II. Dosimetry prior to radioiodine therapy of benign thyroid diseases

Heribert Hänscheid · Cristina Canzi · Wolfgang Eschner · Glenn Flux · Markus Luster · Lidia Strigari · Michael Lassmann

Received: 22 February 2013 / Accepted: 26 February 2013

Abstract The EANM Dosimetry Committee Series "Standard Operational Procedures for Pre-Therapeutic Dosimetry" (SOP) provides advice to scientists and clinicians on how to perform patient-specific absorbed dose assessments. This particular SOP describes how to tailor the therapeutic activity to be administered for radioiodine therapy of benign thyroid diseases such as Graves' disease or hyperthyroidism. Pretherapeutic dosimetry is based on the assessment of the individual ^{131}I kinetics in the target tissue after the administration of a tracer activity. The present SOP makes

EANM Standardisation for dosimetry

Eur J Nucl Med Mol Imaging (2010) 37:1238–1250
DOI 10.1007/s00259-010-1422-4

GUIDELINES

EANM Dosimetry Committee guidelines for bone marrow and whole-body dosimetry

Cecilia Hindorf · Gerhard Glatting · Carlo Chiesa · Ola Lindén · Glenn Flux

Published online: 22 April 2010

Abstract
Introduction The level of administered activity in radionuclide therapy is often limited by haematological toxicity resulting from the absorbed dose delivered to the bone marrow. The purpose of these EANM guidelines is to provide advice to scientists and clinicians on data acquisition and data analysis related to bone-marrow and whole-body dosimetry.

Materials and methods The guidelines are divided into sections "Data acquisition" and "Data analysis". The Data acquisition section provides advice on the measurements required for accurate dosimetry including blood samples, quantitative imaging and/or whole-body measurements with a single probe. Issues specific to given radiopharmaceuticals are considered. The Data analysis section provides advice on the calculation of absorbed doses to the whole

Standardisation

Currently no authority to govern standardisation for therapy (cf ICRU for EBRT)

Lack of dosimetry standardisation often given as an excuse to avoid it

However, more standards in preparation, including:

I-131 mIBG treatment
Lu-177 for adult NETs
Error analysis
Microsphere treatments

Significant boost with input from MetroMRT, and role of European metrology institutes

Rules and regulations

ISSN 1977-0677

Official Journal of the European Union

L 13

English edition

Legislation

Volume 57

17 January 2014

Contents

Rules and regulations

Article 56

Optimisation

1. Member States shall ensure that all doses due to medical exposure for radiodiagnostic, interventional radiology, planning, guiding and verification purposes are kept as low as reasonably achievable consistent with obtaining the required medical information, taking into account economic and societal factors.

For all medical exposure of patients for radiotherapeutic purposes, exposures of target volumes shall be individually planned and their delivery appropriately verified taking into account that doses to non-target volumes and tissues shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose of the exposure.

Rules and regulations

Article 56

Optimisation

1. Member States shall ensure that all doses due to medical exposure for radiodiagnostic, interventional radiology, planning, guiding and verification purposes are kept as low as reasonably achievable consistent with obtaining the required medical information, taking into account economic and societal factors.

For all m
purposes, e
planned ar
account that doses to non-target volumes and tissues shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose of the exposure.

(81) "radiotherapeutic" means pertaining to radiotherapy, including nuclear medicine for therapeutic purposes;

Rules and regulations

Article 56

Optimisation

1. Member States shall ensure that all doses due to medical exposure for radiodiagnostic, interventional radiology, planning, guiding and verification purposes are kept as low as reasonably achievable consistent with obtaining the required medical information, taking into account economic and societal factors.

For all m
purposes,
planned ar
account that doses to non
as low as reasonably a
intended radiotherapeutic

(81) "radiotherapeutic" means pertaining to radiotherapy, including nuclear medicine for therapeutic purposes;

CHAPTER X

FINAL PROVISIONS

Article 106

Transposition

1. Member States shall bring into force the laws, regulations and administrative provisions necessary to comply with this Directive by 6 February 2018.

EANM Internal Dosimetry Task Force

To address the EU directive:

Aim:

1. To review whether it is possible to implement the directive
2. To consider implications of doing so

Survey underway: Number of therapy procedures and administration protocols

Open call for contributors

Feasibility of dosimetry based treatment planning for all radiotherapeutics?

Existing therapy procedures

I-131 NaI for Thyroid Cancer
I-131 NaI for Benign Thyroid Diseases
Y-90 for Non-Hodgkin Lymphoma
I-131 for Non-Hodgkin Lymphoma
Y-90 for Liver Tumors
I-131 mIBG for Neuroblastoma
I-131 mIBG for Adult Neuroendocrine Disease
Lu-177 Radiopeptides for Adult Neuroendocrine Disease
Y-90 Radiopeptides for Adult Neuroendocrine Disease
Re-188 for Benign Bone Diseases
Y-90 for Benign Bone Diseases
Re-186 for Benign Bone Diseases
Er-186 for Benign Bone Diseases
Re-186 for Bone Metastases
Sm-153 for Bone Metastases
Sr-89 for Bone Metastases
Ra-223 for Bone Metastases
P-32 for Myeloproliferative Neoplasms

Prospective therapy procedures

Lu-177 for Prostate Cancer
Ho-166 Microspheres for Intra-arterial Treatment
Re-188 Microspheres for Intra-arterial Treatment
Y-90 Microspheres for Intra-arterial Treatment
Ac-225 for Leukaemia
Bi-213 for Leukaemia
Bi-212 for Leukaemia
Ra-223 for Leukaemia
At-211 for Leukaemia
Tb-149 for Leukaemia
Pb-212 for Leukaemia
Y-90 for Brain Tumors
Y-90 for Breast Cancer
Y-90/Lu-177 for Colorectal Carcinoma
I-131 for Pancreatic Carcinoma
Y-90 for Pancreatic Carcinoma
I-131 for Renal Carcinoma
Sn-117m DTPA Bone Metastases
Th-227 and Other Alpha Emitters

Therapy/diagnostic pairs:

$^{90}Y/^{111}In$

^{131}I / ^{124}I

$^{44}Sc/\ ^{47}Sc$

Conclusion

Dosimetry based treatment planning is mandatory for external beam therapy and for brachytherapy.

It should also be mandatory for therapy with radiopharmaceuticals.

This is a major challenge – scientifically, logistically, politically.

Possibly the most exciting and dangerous time for therapy in nuclear medicine!

The march of time… still smiling…

Michael Lassmann
Manuel Bardies
Myriam Monsieurs
Sven-Erik Strand
Sauli Savolainen
Carlo Chiesa
Mark Konijnenberg
Klaus Bacher
Michael Ljungberg
Katarina Sjogreen-Gleisner
Lidia Strigari
Stig Palm
Gian Luca Poli

EANM congress Hamburg, October 10th – 14th: Do.MoRe 6th International Symposium on DOsimetry and MOlecular Radiotherapy (abstract deadline 27th April)