Radiological Protection of Patient in Nuclear Medicine

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I. A change of paradigm

II. Trend in NM practices

III. Regulations
A change of paradigm: Justification of medical practice

The hierarchy of the justification principle of the radiation protection reveals a change in the paradigm of the radiological protection of patients.

The role of the physician who prescribes the medical practice becomes more relevant, together with the nuclear medicine specialist who should be co-responsible for the application of this justification principle.
Justification of medical practice

It is the 1st step prior for a new medical practice:

• The generic justification

• The individual justification

The individual justification of the medical practice has to be based on the fundamental that the new information will contribute to confirm the diagnosis or to support the therapeutic strategy.
The benefit should be higher than the benefit obtained from other techniques which would involve fewer doses or no exposure to ionizing radiation at all.

In the case of therapeutic medical practice the justification is the physician’s conviction (nuclear medicine specialist) that is the most appropriate treatment for the patient pathology according to all the information from the physician who prescribes it.
A change of paradigm

For doses optimization and the implementation of Dose Reference Level the involvement extends far beyond the Physician and R.P. Officer.

It is clear that the Medical Physicist is to play a very relevant role in the coordination of actions, as the nuclear medicine Technician is to execute them.
Thyroid gland pathologies treatments are still the most extended therapy in nuclear medicine,

But, the field is rapidly expanding:

Other therapies include neuroendocrine tumours, painful skeletal metastases, some arthropathies, polycythaemia, and malignant effusions.

Nuclear medicine treatment options are being investigated in the leukaemias/lymphomas and some liver tumours.
Therapeutic applications

→ thyroid pathologies (hyperthyroidism, tumors)

→ therapy for pain palliation (bone metastases)

→ PRRT (Peptide Receptor Radionuclide Therapy)

→ treatments with alfa-emmiters
Role of patient-specific dosimetry

choice of radionuclides
identification of critical organs
side effects in normal organs
maximum administrable activities
validate the methods to reduce the absorbed doses to critical organs
absorbed dose to the target
Biodistribution

WB images at different times
activity-time curves for source organs
Internal dosimetry steps

- **blood**
- **urine**
- **brain**
- **liver**
- **kidney**
- **heart**
- **lung**
- **ECF**
- **out**

**Software**: OLINDA

**Compartmental model**

**Absorbed doses**

$\tau$
Role of patient-specific dosimetry

Internal dosimetry is critical during phase I and II trials:

• To determine biodistribution
• To establish a dosimetry database
• To examine potential correlations

Even outside of clinical trials may be helpful:

• To customize doses to individual patients
Dosimetry of Therapeutic Agents

There are factors limiting effectiveness of current bone marrow dosimetry techniques:

- Sgouros (i.e. interpat. BM reserve)
- Bolch (i.e. Marrow cellularity)

So that,

90Y ibritumomomab tiuxetan is administrated accordingly 0.4 mCi/kg without previous dosimetry (only biodistribution images)
Dosimetry of Therapeutic Agents

But

- Only for patient who fits screening requirements

- So, I.D. will contribute to expanding the role of $^{90}$Y ibritumomab tiuxetan for others patients who doesn´t meet those requirements
Fast evolution of nuclear medicine therapies

The opportunity of a therapy should be based on absorbed doses in target tissue and in health organs.

There are methods to optimize treatments to reduce the bone marrow dose, bladder, kidney.

Patient specific dosimetry is necessary to determine the optimum activity to administrate.
Targeted radionuclide therapy involves the use of radiolabeled tumor-seeking molecules to deliver a cytotoxic dose of radiation to tumor cells.
PRTT: could dosimetry be helpful?

- To compare absorbed doses predicted for therapy with $^{177}$Lu- and $^{90}$Y- peptides, in view of possible combined therapy

- Is it possible to reduce the absorbed dose to the critical organs?
Choice of radionuclide

**90Y characteristics**
- β energy: 2.3 MeV
- range: \(R_{\text{max}}\) 11 mm
- T1/2 physic: 64 h

**177 Lu characteristics**
- β energy: 0.5 MeV
- range: \(R_{\text{max}}\) 2 mm
- γ energy 1: 113 KeV (6%)
- γ energy 2: 208 KeV (11%)
- T1/2 physic: 6.7 d
**177Lu vs. 90Y absorbed doses**

Median absorbed doses in 10 pts

<table>
<thead>
<tr>
<th>Organ</th>
<th>177Lu-DOTATATE</th>
<th>90Y-DOTATATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidneys</td>
<td>2.1 (∅&lt; 2cm)</td>
<td>4.5 (∅&gt; 2cm)</td>
</tr>
<tr>
<td>Liver</td>
<td>0.5</td>
<td>0.0</td>
</tr>
<tr>
<td>Red Marrow</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Spleen</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Testes</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>U. Bladder</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Other organs</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

**Tumours**

<table>
<thead>
<tr>
<th>90Y</th>
<th>2.1 (∅&lt; 2cm) ... 4.5 (∅&gt; 2cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>177Lu</td>
<td>~ 4</td>
</tr>
</tbody>
</table>
* $^{90}\text{Y}$- vs. $^{177}\text{Lu}$- DOTATATE is able to deliver ~ 4-fold doses to normal organs while dose ratios for lesions ranged from 2.1 ($\varnothing < 2\text{cm}$) to 4.5 ($\varnothing > 2\text{cm}$)

* Benefit/risk balance remains to be established for each patient
Role of patient-specific dosimetry

Is it possible to reduce the absorbed dose to the most irradiated organs and critical organs?
KIDNEYS

critical organs for peptide radionuclide therapies
### Threshold Doses

**External Radiotherapy: Dose-Effect Curves**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Side Effect</th>
<th>TD&lt;sub&gt;5/5&lt;/sub&gt; - TD&lt;sub&gt;50/5&lt;/sub&gt; (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red marrow</td>
<td>aplasia</td>
<td>2.5 - 4.5</td>
</tr>
<tr>
<td><strong>Kidneys</strong></td>
<td><strong>nephropathy</strong></td>
<td><strong>20 - 25</strong></td>
</tr>
<tr>
<td>Liver</td>
<td>hepatitis</td>
<td>25 - 40</td>
</tr>
<tr>
<td>Bladder</td>
<td>collapse</td>
<td>60 - 80</td>
</tr>
</tbody>
</table>

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Kidney uptake in peptide radionuclide therapy

- absorbed dose to kidneys is high and strongly patient-dependent

- acute and delayed kidney toxicity are the major concern for these therapies

In order to protect kidneys, the efficacy of amino acids and of other positively charged molecules has been studied for $^{111}$In-DOTATOC
pharmacokinetics with amino acid protection

Pharmacokinetics is not altered by kidneys protective agents
Kidney uptake with renal protection curves show similar patterns but lower uptake (%) values at all times.
Renal protective drugs enable to consistently reduce the absorbed dose to kidneys.

→ *Therapeutical activities can be increased*, delivering a *cumulative “safe” dose to kidneys* <25 Gy (?)
a further topic about kidney damage / protection

How radiolabeled peptides distribute in kidneys? Is it acceptable to consider a uniform activity uptake?

Or, on the contrary, a specific localization in different renal tissues regions (cortex, medulla) may be significantly outlined?
Role of patient-specific dosimetry

Kidney is a critical organ

• Without previous dosimetry:
  when no attempts at dosimetry were made in the phase of early human use, renal failure cases were reported

• Dosimetry based treatment:
  By infusion of large amount of amino acids, the kidney dose was reduce (20 -40%)

Role of patient-specific dosimetry

Factors that could affect the accuracy of dosimetry:

- kidney volume variability (231 to 503 ml)
- heterogeneous kidney activity distribution (cortex, medulla, pelvis, papillae)

- very low dose rate and low energies:

Kidney toxicity limit:
- 23 Gy (from external beam therapy experiences)
- extrapolation to radiopharmaceutical therapy: 35 Gy
Patient specific dosimetry (*)

THYROID PATHOLOGIES THERAPY

(*) A.C. Traino – Sezione di Fisica Medica, U.O. Fisica Sanitaria, Azienda Ospedaliero-Universitaria Pisana – Pisa (Italy)
131I - HYPERTHYROIDISM THERAPY

Aim of the therapy:

to become eu or hypothyroidism

administering the optimum activity of $^{131}$I needed through patient-specific dosimetry
Significative reduction of thyroid volume (mass) after $^{131}\text{I}$ therapy of Graves’ disease is common and has been reported in literature.

The maximum rate of reduction is during the first month after therapy administration, when $^{131}\text{I}$ is in the gland yet.
Recently an empirical relationship between post-therapeutic thyroid volume (mass) and therapy outcome has been demonstrated by a number of authors [Chiovato et al *JCEM* 83:40-46 (1998); Haase et al *Exp Clin Endocrinol Diabetes* 108:133-137 (2000); Gomez-Arnaiz et al *Horm Metab Res* 35:492-497 (2003)]

POSSIBILITY TO DECIDE THE “OPTIMUM” THERAPEUTIC ACTIVITY BASED ON THE DESIRED REDUCTION OF THYROID VOLUME (MASS) DUE TO $^{131}$I THERAPY
$D_T$ VALUE WHICH CAN REDUCE $m_0$ TO $m_{\text{fin}}=0.1$ g
$A_0$ WHICH CAN REDUCE $m_0$ TO 0.1 g FOR THREE DIFFERENT TARGET UPTAKES

$T_{\text{max}} = 4$ h; $T_{\text{eff}} = 60$ h
The patients have different $^{131}$I kinetics in the target and different target masses to ablate.

What is the best modality to calculate the administered activity?
A new concept of “optimal” dose value comes from a simple theoretical mathematical model: the optimal dose value depends on the individual characteristics of the patient.
OPTIMUM ACTIVITY CHOICE BASED ON FINAL THYROID MASS...

We need

• knowledge of the optimum final-thyroid mass (volume) value

• A model correlating the final thyroid mass to the thyroid absorbed dose (activity)
### $^{131}$I KINETICS BASED ON TWO MEASUREMENTS

<table>
<thead>
<tr>
<th></th>
<th>$U_{24} &gt; U_4$</th>
<th>$U_{24} &lt; U_4$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_{\text{max}}(h)$</td>
<td>$U_{24}/U_4 \leq 0.88$</td>
<td>$0.88 \leq U_{24}/U_4 &lt; 0.92$</td>
</tr>
<tr>
<td>$T_{\text{eff}}(h)$</td>
<td>24 (normal)</td>
<td>4 (quick)</td>
</tr>
<tr>
<td>$U_{\text{max}}$</td>
<td>$U_{24}$</td>
<td>$U_4$</td>
</tr>
</tbody>
</table>
KEYPOINT

This is a new mathematical model for the evaluation of the final mass of thyroid due to $^{131}$I therapy of Graves’ disease:

- It is predictive and relates the administered activity $A_0$ to the final (desired) value of thyroid mass $m_{\text{fin}}$
- It allows to decide the administering activity $A_0$ based on the desired final value of thyroid mass $m_{\text{fin}}$
KEYPOINT

- This model can be used as a new modality to administer the $^{131}$I therapy

- This model can be probably applied to the dosimetry in $^{131}$I therapy of residue/metastasis (thyroid cancer) where it has some important consequences

III. Regulations: too much or not enough?

- the regulator’s role is to ensure that appropriate steps are taken to ensure that misadministrations of radioactive materials and involuntary exposures of medical staff and of the public are minimized.

- for example, exposures of visitors of patients who have radioactive substances in their bodies.

- It is these unintended exposures that justify regulation.
III. Regulations: too much or not enough?

- The challenge for the regulator is to establish a regulatory structure that serves to minimize these unintended risks, while also avoiding undue interference in medical judgments.
III. Regulations: too much or not enough?

• Too much regulation can result in the needless delay of medical or technological advances, higher health care costs, or ineffective patient care.

• Too little regulation can lead to an increase in misadministrations and increased likelihood that patients, medical staff, and the public will receive involuntary exposures.

• A careful balance must be attained in establishing an appropriate regulatory regime.
III. Regulations: too much or not enough?

- Regulation should provide the appropriate vehicle for reducing radiation risks,

  while also

- minimizing interference with the beneficial uses of medicine.
Conclusions

• Patients given therapy with internal emitters do not deserve a lower standard of care than those treated with external radiation.

• Patient-specific dosimetry is needed:
  - To bring radiation therapy with internal emitters to the same level of quality and detail as with external sources
  - To provide reliable dose information that will predict radiation effects – in major organs and marrow

• Much more specific internal dosimetry training should be done
Finally….

The radiation protection of patients in nuclear medicine should be improved.

It requires on a multidisciplinary approach
Thank you very much!

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