Current issues and trends in brachytherapy; a medical physics perspective

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Anniversary Paper: Past and current issues, and trends in brachytherapy physics

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4708 Med. Phys. 35 (10), October 2008
Table III. Overview of all AAPM reports on brachytherapy, with report number and year of publication

<table>
<thead>
<tr>
<th>Report Number</th>
<th>Year of Publication</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>1987</td>
<td>Radiation Therapy Committee Task Group #32. Specification of Brachytherapy Source Strength.</td>
</tr>
<tr>
<td>51</td>
<td>1995</td>
<td>Radiation Therapy Committee Task Group #43. Dosimetry of Interstitial Brachytherapy Sources.</td>
</tr>
<tr>
<td>61</td>
<td>1998</td>
<td>Radiation Therapy Committee Task Group #59. High Dose-Rate Brachytherapy Treatment Delivery.</td>
</tr>
<tr>
<td>66</td>
<td>1999</td>
<td>Radiation Therapy Committee Task Group #60. Intravascular Brachytherapy Physics.</td>
</tr>
<tr>
<td>68</td>
<td>1999</td>
<td>Radiation Therapy Committee Task Group #64. Permanent Prostate Seed Implant Brachytherapy.</td>
</tr>
</tbody>
</table>

Since 1995...7 other AAPM task groups active...(per 2009)
Evolution in afterloading equipment

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Trends in patient numbers

Perhaps due to the attraction of a 1 day procedure along with a favorable profile of normal tissue complications, the number of procedures has grown from less than 5000 in 1995 to between 40 000 and 60 000 in 2002. This is approximately 30% to 40% of all eligible patients diagnosed annually in the United States. (Thomadsen et al 2008)

Dutch GEC-ESTRO PCB participation 2002-2007

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Present status of brachytherapy:

Pro:
- 100 years of experience,
- ability to deliver high equivalent dose / fraction,
- high targeting accuracy,
- target conformity, low normal tissue dose
- small/negligible inter/intrafraction movement and therefore smaller margins,
- relatively low costs
Present status of brachytherapy:

Con:

- challenged by other modalities,
- vendor’s research aimed at external beam therapy,
  
  BT developments often only “followed”,
- invasive,
- inhomogeneous dose distribution
Some “physics” issues to be discussed:

- Sources,
- Afterloading equipment,
- Applicators,
- Treatment planning,
- Imaging,
- Calibration of sources
“Physics” issues: Sources (general)

Design requirements:
• sealed safely, rigid construction,
• photon energy suitable for the purpose (HDR),
• high specific activity (HDR),
• suitable half life,
• visibility on imaging,
• isotropic dose delivery,
• calibration standard available,
• low costs
Some properties of radionuclides in afterloading
Co-60, renewed interest; Yb-169 and Tm-170 low γ’s

<table>
<thead>
<tr>
<th>Isotope name</th>
<th>Brachytherapy sources comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cobalt-60</td>
<td>Ceasium-137</td>
</tr>
<tr>
<td>Iridium-192</td>
<td>Ytterbium-169</td>
</tr>
<tr>
<td>Thulium-170</td>
<td>Iodine-125</td>
</tr>
<tr>
<td>Palladium-103</td>
<td></td>
</tr>
<tr>
<td>Short</td>
<td>Co-60</td>
</tr>
<tr>
<td></td>
<td>Cs-137</td>
</tr>
<tr>
<td></td>
<td>Ir-192</td>
</tr>
<tr>
<td></td>
<td>Yb-169</td>
</tr>
<tr>
<td></td>
<td>Tu-170</td>
</tr>
<tr>
<td></td>
<td>I-125</td>
</tr>
<tr>
<td></td>
<td>Pd-103</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Properties:</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparable activity</td>
<td>370 GBq/10Ci</td>
<td>/25Ci</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Photon energy range</td>
<td>1170 -1330 KeV</td>
<td>200 - 1060 KeV</td>
<td>50 - 308 KeV</td>
<td>48 - 84 KeV</td>
<td>27 -41 KeV</td>
<td>20,1 - 23 Kev</td>
<td></td>
</tr>
<tr>
<td>Mean photon energy</td>
<td>662 Kev</td>
<td>380 Kev</td>
<td>93 Kev</td>
<td>84 Kev</td>
<td>28 Kev</td>
<td>21 Kev</td>
<td></td>
</tr>
<tr>
<td>Half-life</td>
<td>5,3 Years</td>
<td>30,2 years</td>
<td>74,0 days</td>
<td>32,0 days</td>
<td>128 days</td>
<td>59,4 days</td>
<td>17,0 days</td>
</tr>
<tr>
<td>Maximum specific activity</td>
<td>15,5 GBq/mm</td>
<td>340 GBq/mm²</td>
<td>23,8 GBq/mm²</td>
<td>132 GBq/mm³</td>
<td>230 GBq/mm³</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chargable content</td>
<td>1.0 %</td>
<td>3.1 %</td>
<td>14,90%</td>
<td>21%</td>
<td>4,50%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chargable content enriched</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Half value layer in lead</td>
<td>10 mm</td>
<td>6,5 mm</td>
<td>6,0 mm</td>
<td>2,6 mm</td>
<td>0,25 mm</td>
<td>0,03 mm</td>
<td>0,02 mm</td>
</tr>
<tr>
<td>Tenth value layer in lead</td>
<td>16 mm</td>
<td>8,6 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concrete wall of treatment room</td>
<td>40 cm</td>
<td>23 cm</td>
<td>15cm</td>
<td>4,5 cm</td>
<td>1 cm</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Current issues and trends in brachytherapy;
a medical physics perspective
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Courtesy Isodose Control
“Physics” issues: Sources

Physics properties in some of these “new” HDR sources

- Co-60: high specific activity; long half life; requires high radiation protection; low costs,
- Yb-169: low half life; low energy, simple radiation protection; high costs,
- Tm-170: suitable half life; low energy, simple radiation protection; beta component; low specific activity
Comparison of the dosimetric characteristics of Ir-192 vs Co-60 HDR sources

Essentially: these differences are negligible
“Physics” issues: Sources for permanent LDR

- Low energy required, <= 50 keV for radiation safety,
- visibility on imaging,
- calibration to be guaranteed,
- stable and reliable delivery system,
- approved RPC registration for availability of TG-43U1 recommended data set

“Non-physics” issues:

- High “volume”, commercially very interesting for the vendors => strong competition (note: more than 20 models proposed!),
- packaging: seed cartridges, pre-loaded needles and catheters,
- uniform and customized non-uniform spaced source strands,
- automated needle loading systems

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Alternative to $^{125}$I and $^{103}$Pd

Cs-131 decay scheme:

$^{131}$Cs

9.689 d

5/2+

0

$^{131}$Xe

stable

3/2+

0

100%

5.5

short half life,

decays by electron capture to Xe-131 followed by characteristic x-ray emission,

4-34 keV photons,

average 30 keV
OncoSeed 6701/02
EchoSeed 6733
OncoSeed 6711 (also IsoAid)
TheraSeed 200

Designs of seeds

Courtesy R. Nath, AAPM summerschool 2005
“Physics” issues: Afterloading equipment

Design requirements:
- radiation safety,
- fail safe in use,
- 1 or 2 sources (? , pending national regulations),
- small source size,
- number of channels,
- practical length of source trajectory,
- (costs, service system,...)
Realised in modern design of afterloader equipment

- dual or multi-source capability,
- HDR and PDR functionality
- electronic brachytherapy (not discussed today)
Table 2.1 Specific features of high dose rate afterloading devices. Updated from Glasgow and Anderson (1994). Note that the GammaMed systems are now marketed by Varian Med. Sys. Inc. In general, further developments in the latest versions of the equipment have led especially to smaller source diameters.

<table>
<thead>
<tr>
<th>Manufacturer or vendor</th>
<th>Varisource 200 series (Varian Medical Systems Inc., USA)</th>
<th>MicroSelectron HDR (Nucletron, The Netherlands)</th>
<th>GammaMed 12i (Varian Medical Systems Inc., USA)</th>
<th>GammaMed Plus (Varian Medical Systems Inc., USA)</th>
<th>Omnitron 2000 (Omnitron Corpor., USA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) No of sources and container max storage activity</td>
<td>1 x 44 mGy·h⁻¹ @ 1 m</td>
<td>1 x 40 mGy·h⁻¹ @ 1 m</td>
<td>1 x 80 mGy·h⁻¹ @ 1 m</td>
<td>1 x 60 mGy·h⁻¹ @ 1 m</td>
<td>1 x 48 mGy·h⁻¹ @ 1 m</td>
</tr>
<tr>
<td>b) Physical size, OD = outer diameter, L = active length</td>
<td>0.59 mm OD 5 mm L</td>
<td>1.1 mm OD 5 mm L</td>
<td>1.1 mm OD 6.5 mm L</td>
<td>0.9 mm OD 3.5 mm L</td>
<td>0.59 mm OD 10 mm L</td>
</tr>
<tr>
<td>Smallest outside diameter of applicators</td>
<td>0.81 mm</td>
<td>1.4 mm</td>
<td>1.6 mm</td>
<td>1.4 mm</td>
<td>0.89 mm</td>
</tr>
<tr>
<td>Method of source attachment</td>
<td>Embedded in the Nitinol (Nickel-Titanium) source drive wire</td>
<td>Laser welded to drive cable</td>
<td>Welded to steel drive cable using a special weld technique</td>
<td>Laser welded to drive cable</td>
<td>Permanently connected to Pt wire</td>
</tr>
<tr>
<td>Maximum source extension</td>
<td>1,500 mm</td>
<td>1,500 mm</td>
<td>1,250 mm</td>
<td>1,300 mm</td>
<td>1,500 mm</td>
</tr>
<tr>
<td>No of applicator channels</td>
<td>20</td>
<td>18</td>
<td>24</td>
<td>24</td>
<td>10</td>
</tr>
<tr>
<td>Method of source movement</td>
<td>Step-back, 20 steps 2-99 mm step size in 1 mm increments</td>
<td>Step-forward, 48 steps of 2.5 mm over 12 cm; 5 mm over 24 cm</td>
<td>Step-back, 40 steps to 40 cm; 1 mm to 10 mm steps</td>
<td>Step-back, 60 steps 1-10 mm step size in 1 mm increments</td>
<td>Step-back, in 11 mm increments over 20 cm</td>
</tr>
</tbody>
</table>

**HDR Afterloaders (a basic comparison; this needs an update!)**

See [www.estro.org](http://www.estro.org) under publications, physics booklet 8

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“Physics” issues: Applicators

- Surface applicators, e.g. Leipzig applicator,
- Deeper treatments into tissue, e.g. to the breast, e.g. AccuBoost,
- MammoSite breast balloon technique, and new designs for improved skin sparing, NAS Medical ClearPath, Contura/SenoRx Inc,
- Plastic composition of many new applicators, allows steam sterilisation, better compatibility with imaging requirements, MR visibility,
New approaches in applicators

AccuBoost

For image guided breast irradiation

‘Leipzig’ applicator

Contura

SenoRx

NAS Medical, ClearPath

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refinements in applicators

New features in these applicators: flexibility, fixation, light-weight, MR compatible (titanium), smaller, …
Modified MRI compatible Stockholm based standard tandem-ring applicator-Nucletron ®

Combinations of intracavitary and interstitial

MRI-compatible vaginal cylinder + tandem + template for plastic needles
“Physics” issues: Treatment Planning
(TG-43 is the standard)
Developed @ AAPM, published 1995 Med Phys

Why this formalism???

- introduction of revised calibration standards,
- source strength specification quantities,
- dose calculation formalisms,
- confusion with regard to dosimetric data,
- only quantities from dose rates in water medium near the actual source to be used
TG-43 formalism in a nutshell

\[ \dot{D}(r, \theta) = S_K A \frac{G(r, \theta)}{G(r_0, \theta_0)} g(r) F(r, \theta) \]

5 x Multiplications
1 x division

But... where to find these data??

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CourtesY Baltas

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## Dosimetry Datasets

### Joint AAPM/RPC Registry of Brachytherapy Sources

**Meeting the AAPM Dosimetric Prerequisites**

### $^{125}\text{I}$ Sources

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Sources</th>
<th>Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amersham</td>
<td>OncoSeed</td>
<td>6711</td>
</tr>
<tr>
<td>BEBIG GmbH</td>
<td>IsoSeed® I-125</td>
<td>I25.S06</td>
</tr>
<tr>
<td>Best Industries</td>
<td>Best@ I-125 Source</td>
<td>I25.S06</td>
</tr>
<tr>
<td>IBt</td>
<td>Intersource$^{125}$</td>
<td>1251L</td>
</tr>
<tr>
<td>IsoAid, LLC</td>
<td>Advantage I-125</td>
<td>IAI-125A</td>
</tr>
<tr>
<td>Core Oncology, Inc.</td>
<td>ProstaSeed ®</td>
<td>125SL 125SH</td>
</tr>
<tr>
<td>North American Scientific</td>
<td>Prospera I-125</td>
<td>Med 3631-A/M</td>
</tr>
<tr>
<td>Nucletron</td>
<td>SelectSeed I-125</td>
<td>130.002</td>
</tr>
<tr>
<td>Bard Urological Division</td>
<td>$^{125}$ Implant Seeds</td>
<td>STM1251</td>
</tr>
<tr>
<td>Theragenics Corporation$^\text{®}$</td>
<td>I-Seed I-125</td>
<td>I25.S06</td>
</tr>
</tbody>
</table>

### $^{103}\text{Pd}$ Sources

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Sources</th>
<th>Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best Medical International Inc</td>
<td>Best Palladium - 103</td>
<td>2335</td>
</tr>
<tr>
<td>IsoAid, LLC</td>
<td>Advantage Pd-103</td>
<td>IAPd-103A</td>
</tr>
<tr>
<td>North American Scientific</td>
<td>Prospera Pd -103</td>
<td>Med 3633</td>
</tr>
<tr>
<td>Theragenics Corporation$^\text{®}$</td>
<td>TheraSeed$^\text{®}$</td>
<td>200</td>
</tr>
</tbody>
</table>

### $^{131}\text{Cs}$ Sources

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Sources</th>
<th>Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>IsoRay Medical Inc.</td>
<td>Proxcelan</td>
<td>Cs - 1</td>
</tr>
</tbody>
</table>

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**Current issues and trends in brachytherapy; a medical physics perspective**  
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Estro provides Physics data:
- TG43,
- radiation protection data brachytherapy sources

Or see: RPC website, or Taylor&Rogers, Carleton Univ

One can take it from web based presentation of data, e.g.:

www.estro.org

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“Physics” issues: Treatment Planning

But: the present-day TG-43 formalism is not ideal:

- differences between absorbed dose in the water and tissue,
- differences between radiation attenuation in water and tissue,
- source shielding or applicator radiation interactions,
- differences between radiation scattering for dataset acquisition and patient treatment,
- subtleties in the difference between dose and kerma, and not accounting for emitted electrons
“Physics” issues: Treatment Planning

These flaws in TG-43 may contribute to uncertainties, depending on the specific situation, in the order of up to 10% in dose deposition

There is a need for a new approach in dose calculation, choices are from:

- direct Monte Carlo based,
- analytical Models, leading to convolution superposition algorithms (Monte Carlo supported primary/scatter separation),
- deterministic solution to the transport equation

New (international) TG-186 group under AAPM BTSC “Model-Based Dose Calculation Techniques in Brachytherapy: Status and Clinical Requirements for Implementation Beyond AAPM TG-43”. The aim is to review the potential next generation brachytherapy dose calculation algorithms, and to provide guidance for early adopters in using model-based dose calculation algorithms in brachytherapy, especially for commissioning, handling of patient data, and prescription and dose scoring.
“Physics” issues: Introduction of 3D image guided brachytherapy

Requires
- suitable imaging equipment,
- special applicators,
- reconstruction,
- analysis of each step of the procedure,
- re-assessment of uncertainties,
- careful evaluation of the new clinical results
<table>
<thead>
<tr>
<th>Tissue</th>
<th>1st choice</th>
<th>2nd choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobile Tongue</td>
<td>MRI</td>
<td>CT</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>MRI</td>
<td>CT</td>
</tr>
<tr>
<td>Buccal mucosa</td>
<td>MRI, CT, US</td>
<td>CT, US (endo)</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>MRI, ES</td>
<td>CT, US (endo)</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>ES, MRI (CT)</td>
<td>CT</td>
</tr>
<tr>
<td>Lip</td>
<td>MRI</td>
<td>CT</td>
</tr>
<tr>
<td>Cervix</td>
<td>MRI</td>
<td>CT</td>
</tr>
<tr>
<td>Endometrium</td>
<td>MRI, ES</td>
<td>CT</td>
</tr>
<tr>
<td>Vagina</td>
<td>US (endo), MRI</td>
<td>CT, US (endo)</td>
</tr>
<tr>
<td>Breast</td>
<td>Mammography, MRI, ES, MRI, CT</td>
<td>CT, US</td>
</tr>
<tr>
<td>Bladder</td>
<td>ES, MRI</td>
<td>US, CT</td>
</tr>
<tr>
<td>Prostate</td>
<td>MRI</td>
<td>CT</td>
</tr>
<tr>
<td>Penis</td>
<td>MRI, ES, MRI, US (endo)</td>
<td>CT, MRI, US (endo)</td>
</tr>
<tr>
<td>Anorectal</td>
<td>ES, MRI, US (endo)</td>
<td>CT, US, MRI</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>ES, Oesophagogram (Barium)</td>
<td>CT</td>
</tr>
<tr>
<td>Bile duct</td>
<td>Cholangiogram, ES, MRI</td>
<td>CT</td>
</tr>
<tr>
<td>Soft tissue sarcoma</td>
<td>ES, CT, Chest X Ray (US)</td>
<td>CT</td>
</tr>
<tr>
<td>Bronchus</td>
<td>MRI</td>
<td>MRI</td>
</tr>
<tr>
<td>Skin</td>
<td>fundoscopy, US, angiography</td>
<td>CT</td>
</tr>
<tr>
<td>Brain</td>
<td>MRI</td>
<td>MRI</td>
</tr>
<tr>
<td>Eye</td>
<td>fundoscopy, US, angiography</td>
<td>CT</td>
</tr>
<tr>
<td>Intravascular</td>
<td>Angiography, US (IVUS)</td>
<td>MRI</td>
</tr>
</tbody>
</table>

Table 5.2: Overview of imaging procedures for delineation of the Gross Tumour Volume and for determination of the Clinical and Planning Target Volume for different sites of brachytherapy; Endoscopy (ES) is added, if indicated.

From the GEC-ESTRO Handbook of Brachytherapy

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Required infrastructure

GEC-ESTRO Handbook of Brachytherapy
See www.estro.org
Image Guided Brachytherapy

Basic Issues

- "CTV is equal to PTV": no or minor geometric uncertainties
  Applicators/sources move with the target as they are fixed in/to the target tissue

- **Internal Organ motion and changes induced by intervention**
  represent major uncertainties:
  - oedema (prostate/Gyn),
  - organ filling status: bladder, rectum, sigmoid, bowel,
  - organ movement: sigmoid, bowel

- **No classical set-up uncertainties! (applicator reconstruction)**
Opens a completely new field for an „uncertainty analysis“

- Applicator reconstruction
- Interapplication variation
  - If imaging is not performed for every insertion
- Interfraction variation
  - If two or more fractions are based on one insertion and one treatment plan,
  - Variation between imaging and dose delivery,
  - LDR and PDR brachytherapy,
  - Fractionated HDR brachytherapy (prostate/Gyn)
Example: **Interapplication variation**

<table>
<thead>
<tr>
<th></th>
<th>Rectum</th>
<th>D$_{2cc}$</th>
<th>ICRU</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1$^{st}$ fraction</strong></td>
<td>4.7</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td><strong>4$^{th}$ fraction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>plan of 1$^{st}$ frac.</td>
<td>8.3</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>individual plan</td>
<td>4.9</td>
<td>3.6</td>
<td></td>
</tr>
</tbody>
</table>
STANDARD LOADING PATTERN

Optimised Loading Pattern

Kirisits et al. IJROBP 2005

MTD 3.7 Gy

V100 94%
D90 7.9 Gy

D2cc
Rectum 6.7 Gy
Sigma 6.8 Gy

MTD 3.7 Gy

V100 92%
D90 7.4 Gy

D2cc
Rectum 3.4 Gy
Sigma 4.5 Gy
Image guided adaptive brachytherapy (IGBT) cervix cancer local control and cancer specific survival (1998-2003) TREATMENT PERIOD (-/+ IGBT) AND TUMOUR SIZE

mean 81 Gy vs. 90 Gy in HR CTV

Pötter R. et al  Radiother Oncol 2007
“Physics” issues: calibration of sources

- New step to be made: Dose-to-water calibration
- New research activity in the EURAMET network iMERA joint research project #6 on brachytherapy
  - primary standard of absorbed dose to water for 192Ir to be available at three NMIs, and similarly for 125I available at four NMIs in about three years
  - PTB has performed ad hoc intercomparisons of 125I and 103Pd seeds with the University of Wisconsin ADCL

- Requirement is that such a new approach should at least give the same, but preferably, lower source calibration uncertainties

- Needs uniformly transition to develop dose-to-water standards world-wide, and similarly and even important to disseminate these standards to the clinical source users.
FUTURE UNCERTAINTY:

\[ u' = f(u'_1, u'_2, u'_3, u'_4) \]

the future uncertainty \( u' \) is lower than the current uncertainty \( u \)

Accurate determination of the 3D dose distribution

Brachytherapy sources calibrated in terms of absorbed dose to water, \( D_w \), at 1 cm

Transfer standards calibrated in terms of \( D_w \) at 1 cm

Courtesy Maria Pia Toni
Our view:
What is the real development in all this?

The step towards the 3D image guided brachytherapy makes the difference

What matters is the demonstrated improvement in clinical outcome!
All these developments necessitate clearly updating the existing reports by ICRU:


and


Not addressed in ICRU 58:
- Seed types of implant
- Implication of imaging technique
- Margin concepts
- Optimization
- “Dose painting”
- Reporting parameters
A few recent survey papers for further reading:


Future? Integral solutions, aiming at full intra operative treatments….

Thank you for your attention