Roles of In-Vivo Dose Verification in Radiation Therapy

-- PHOTON THERAPY --

Sam Beddar, Ph.D., FCCPM, FAAPM
Professor & Chief of Research

Department of Radiation Physics
The University of Texas MD Anderson Cancer Center
Is there a need for *In Vivo* Dosimetry?

### Table 1. Recent accidents in radiotherapy in France.

<table>
<thead>
<tr>
<th>Where</th>
<th>Year/period</th>
<th>Patients involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>2003</td>
<td>1</td>
</tr>
<tr>
<td>Case 2</td>
<td>2004</td>
<td>1</td>
</tr>
<tr>
<td>Case 3</td>
<td>2004</td>
<td>1</td>
</tr>
<tr>
<td>Case 4.1</td>
<td>May 2004–May 2005</td>
<td>24</td>
</tr>
<tr>
<td>Case 4.2</td>
<td>2001–2006</td>
<td>397</td>
</tr>
<tr>
<td>Case 4.3</td>
<td>1987–2000</td>
<td>312</td>
</tr>
<tr>
<td>Case 5</td>
<td>April 2006–April 2007</td>
<td>145</td>
</tr>
</tbody>
</table>

...ability or complications or reduced probability of tumour control...
Is there a need for *In Vivo* Dosimetry?
IMRT (8 angles)
Axial and sagittal dose distribution
PROSTATE MOTION results in INTER-fraction errors

25 treatment CTs acquired during a course of 42 Txs
What we want to avoid

rectal ulcer

Courtesy of Andrew Lee, M.D.
In Vivo Dosimetry

2008 WHO Report summarized widely reported radiation therapy incidents.
• 3125 Major Incidents (1976-2007)
• 4616 Near Misses (1992-2007)
What are the challenges?

- The energy response of the detectors available at hand.
- The need for precise detector positioning, especially in high-dose gradient regions.
- The large range of doses and dose rates encountered in external beam radiation therapy EBRT or brachytherapy.

Therefore

- IVD is mostly used for legal purposes or reimbursement issues
- or to prevent (rare) major incidents in treatment delivery and used with action levels above 10 - 20 % depending on the site

However, we need to move forward and change the role of IVD by taking it to a higher level.
A quick highlight of current detectors.
State of the Art Detectors: TLDs

- Skin dose measurement for EBRT and HDR breast implants
- Monitoring implanted devices: Implantable pulse generators or cardioverter defibrillators
- LiF rods are the most commonly used for brachytherapy
- Prostate, urethral and rectal dose measurements in HDR prostate implants
State of the Art Detectors: TLDs

**Advantages**
- Different shapes & materials
- No angular dependence
- Not attached to any wire/cable
- Well studied

**Disadvantages**
- Require special preparation (annealing, individual calibration, careful handling, fading correction)
- Read-out process post-irradiation
- Not for online dosimetry
State of the Art Detectors: Alanine

- Chemical detector
- Requires electron paramagnetic resonance (EPR) for read-out
- Few reports on IVD during gynecological treatments
**State of the Art Detectors: Alanine**

**Advantages**
- Almost independent of energy
- Not attached to any wire/cable
- Non-destructive read-out

**Disadvantages**
- Expensive EPR equipment and not easily available in clinic
- Tedious read-out process
- Insensitive to doses < 2 Gy
- **Not for online dosimetry**

_EPR: Electron Paramagnetic Resonance_
State of the Art Detectors: Diodes

- Silicon-based solid-state dosimeters
- Mostly used for EBRT for different purposes (i.e. right wedges, etc...)
- 5-diode arrays used as rectal and bladder dosimeters
- Overall uncertainty in phantom of 7-10%
State of the Art Detectors: Diodes

**Advantages**
- Immediate read-out
- High sensitivity
- Good mechanical stability
- Fairly small size
- Available in arrays

**Disadvantages**
- Angular dependence
- Energy dependence
- Temperature dependence
- Changes in sensitivity with radiation
State of the Art Detectors: MOSFETs

- Metal-oxide-semiconductor field-effect transistor (MOSFET) based on silicon
- Mostly used for monitoring urethral dose in seeds implant
- Uncertainty of 8%
State of the Art Detectors: MOSFETs

**Advantages**
- Small size (can be inserted in catheters)
- Available in arrays
- ~ No angular dependence

**Disadvantages**
- Not water-equivalent
- **Limited life-time**
- Temperature dependence
- Response degrades with accumulated exposure
State of the Art Detectors: RL/OSLDs

• Generally composed of $\text{Al}_2\text{O}_3$:$\text{C}$
• RL: Radoluminescence
• Previously used also as RL/OSLD: Optically stimulated luminescence dosimeter
• Prevention and identification of dose delivery errors in cervix, gynecological and prostate HDR and PDR brachytherapy
• Potential to detect interchanged guide tube errors and source mispositioning
State of the Art Detectors: RL/OSLDs

Advantages
• Small size
• RL feedback in real-time
• Passive/active detector
• Good reproducibility (1.3%)

Disadvantages
• Not water-equivalent
• Stem effect (Cerenkov)
• Small temperature dependence
State of the Art Detectors: PSDs

- PSD: Plastic scintillation detector made of polystyrene, PVT or PMMA
- Coupled to an optical fiber, the stem effect has to be subtracted
- Phantom studies showed excellent dose measurement accuracy
State of the Art Detectors: PSDs

**Advantages**
- Linearity to dose/dose-rate
- Small size
- Energy independence
- Water-equivalence
- No angular dependence
- Real-time dosimetry
- New commercial detectors are emerging

**Disadvantages**
- Stem effect (Cerenkov)
- Small temperature dependence
State of the Art Detectors: EPIDs

- **EPIDs**: Electronic portal imaging devices – flat panel detector commonly based on amorphous silicon photodiode technology
- Developed for acquiring megavoltage portal images during treatments, mainly for determining setup errors
- Back-projection models have been used to reconstruct 3D dose distributions in patients during IMRT and VMAT
State of the Art Detectors: EPIDs

**Advantages**

- Real-time 2D and 3D dose information
- Non-invasive in vivo dosimetry
- Good reproducibility (< 1%)

**Disadvantages**

- Many correction factors (Mijnheer, et al 2013)
- Over-sensitive to low-E photons (response dependence on off-axis beam-hardening effects, patient/phantom thickness in beam)
- Ghosting (non-linearity with dose)
Requirements of IVD

• Minimal to no need for energy response corrections
• Tissue or water-equivalent materials – *would be nice to have*
• High spatial resolution and precise positioning to account for the high dose gradients regions.
  – High dose gradients magnify the effect of positional uncertainty on dosimetric uncertainty.
• High dynamic range to account for varied doses and dose rates.
• Real-time monitoring of the dose delivery – Detectors
• On line monitoring of the dose delivery – Visual Screen
Additional Requirements of IVD

• It’s not enough for a detector to be just suitable for a specific application: EBRT, Brachytherapy or Protons. We need to push IVD to the next level by focusing on detector systems that would also have these additional properties as well.

• Real time feedback
  – Catch errors as they occur and minimize adverse outcomes.

• Well integrated with the clinical workflow
  – Too much extra work for therapists or the physicists will discourage adoption.

• Invisible to the patient as much as possible

• Dose monitoring at multiple locations
  – Line detectors, planar detection, volumetric (???)
In vivo dosimetry (IVD) is in use in external beam radiotherapy (EBRT) to detect major errors, to assess clinically relevant differences between planned and delivered dose, to record dose received by individual patients, and to fulfill legal requirements. After discussing briefly the main characteristics of the most commonly applied IVD systems, the clinical experience of IVD during EBRT will be summarized. Advancement of the traditional aspects of in vivo dosimetry as well as the development of currently available and newly emerging noninterventional technologies are required for large-scale implementation of IVD in EBRT. These new technologies include the development of electronic portal imaging devices for 2D and 3D patient dosimetry during advanced treatment techniques such as IMRT and VMAT, and the use of IVD in proton and ion radiotherapy by measuring the decay of radiation-induced radionuclides. In the final analysis, we will show in this Vision 20/20 paper that in addition to regulatory compliance and reimbursement issues, the rationale for in vivo measurements is to provide an accurate and independent verification of the overall treatment procedure. It will enable the identification of potential errors in dose calculation, data transfer, dose delivery, patient setup, and changes in patient anatomy. It is the authors’ opinion that all treatments with curative intent should be verified through in vivo dose measurements in combination with pretreatment checks.

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Key words: in vivo dosimetry, external beam radiotherapy, detector characteristics, patient safety, dose verification
In vivo dosimetry in brachytherapy

Kari Tanderup
Department of Oncology, Aarhus University Hospital, Aarhus 8000, Denmark and Department of Clinical Medicine, Aarhus University, Aarhus 8000, Denmark

Sam Beddar
Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas 77030

Claus E. Andersen and Gustavo Kertzschker
Center of Nuclear Technologies, Technical University of Denmark, Roskilde 4000, Denmark

Joanna E. Cygler
Department of Physics, The Ottawa Hospital Cancer Centre, Ottawa, Ontario K1H 8L6, Canada

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In vivo dosimetry (IVD) has been used in brachytherapy (BT) for decades with a number of different detectors and measurement technologies. However, IVD in BT has been subject to certain difficulties and complexities, in particular due to challenges of the high-gradient BT dose distribution and the large range of dose and dose rate. Due to these challenges, the sensitivity and specificity toward error detection has been limited, and IVD has mainly been restricted to detection of gross errors. Given these factors, routine use of IVD is currently limited in many departments. Although the impact of potential errors may be detrimental since treatments are typically administered in large fractions and with high-gradient-dose-distributions, BT is usually delivered without independent verification of the treatment delivery. This Vision 20/20 paper encourages improvements within BT safety by developments of IVD into an effective method of independent treatment verification. © 2013 American Association of Physicists in Medicine. [http://dx.doi.org/10.1118/1.4810943]

Key words: in vivo dosimetry, brachytherapy, treatment errors, quality assurance
Real-time IVD systems with a future in EBRT or BT

The items are rated according to good/adequate (+) and inconvenient (-)

<table>
<thead>
<tr>
<th>Properties</th>
<th>MOSFET</th>
<th>RL</th>
<th>PSD</th>
<th>EPID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size/positional resolution</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Sensitivity to dose</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Energy dependence</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Angular/off-axis dependence</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Online dosimetry</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

**Main advantages**
- Small size
- Commercial system at reasonable prize
- High sensitivity
- No angular dependence
- No energy dependence
- 2D and 3D dose distributions
- Permanent record

**Main disadvantages**
- Limited life
- Energy dependence
- Stem effect
- Needs frequent calibration
- Not commercially available
- Stem effect
- Cost
- Limited availability of commercial software

REAL-TIME ACCURACY
The effect of positional uncertainty on dosimetric uncertainty depends highly on the dose gradient.

**Diagram:**

- **Normalized Dose**
  - X-axis: Position (cm) ranging from -6 to 0
  - Y-axis: Normalized Dose ranging from 0% to 100%

- **Uncertainties:**
  - $\Delta Dose = \pm 0.5\%$
  - $\Delta Dose = \pm 2.0\%$
  - $\Delta Dose = \pm 9.0\%$

- **Positional Uncertainty:**
  - $\Delta x = \pm 1\text{mm}$
New Detector Technology

- Multi-point Plastic Scintillation Detector (mPSD)
- Measures dose at multiple points simultaneously with one optical fiber.
- Can track source position during HDR/PDR BT.
- Real time capability.
- Small enough to fit in catheters.

APPLICATION SPECIFIC PSDs
Let the REVOLUTION BEGIN...
OARtrak™ TRUE Adaptive Radiation Therapy

- In vivo Real Time Radiation Dose Data
- Monitors Dose Rate, Dose per Field, Accumulative Dose, Average Dose
- Multiple Sensors for Dose Monitoring of Seminal Vesicles and Apex of Rectal Prostatic Interface
- QA for Intra-fractional Radiation Safety with Dose Verification
- Accumulative OAR Dose Data to Adjust Inter-fractional Treatment
- Hypofractionated Treatment OAR Monitoring
- Easy User Interface with Data Report Export to EMR
EPID systems

Implementation of An Efficient Workflow for the Analysis of Alerts Observed During Large Scale EPID-Based 3D In Vivo Dosimetry
B Mijnheer*, A van Mourik, I Olaciregui Ruiz, A Mans, The Netherlands Cancer Institute, Amsterdam, The Netherlands

**Presentations**
SU-K 205-10 (Sunday, July 30, 2017) 4:00 PM – 6:00 PM Room: 205

**Purpose:** In our institution, more than 3000 RT treatments per year are verified using EPID-based 3D in vivo dosimetry. With our current set of tolerance levels, deviations are detected in about 20% of the treatments. The purpose of this study is to investigate the usefulness of a newly developed workflow to analyze the alerted treatments.

**Methods:** In the new workflow, in vivo reports are automatically created almost immediately after treatment delivery. If no deviation is detected, the treatment is automatically approved. In case of an alert, the new framework links extra sources of information (e.g., cone-beam CT and trends per patient) and imposes treatment-site specific checks to help medical physicists to explain the reason of deviation. In cases where the clinical relevance of a deviation is still in doubt, the workflow prompts the scheduling of extra actions such as EPID or ion chamber based 3D phantom dosimetry. Radiation oncologists and therapists can be consulted at various levels during this workflow.

**Results:** In 2016 about 20 alerts had to be analyzed daily by a medical physicist requiring one to two hours. From these alerted deviations, 83% could immediately be explained following the protocol of the workspace, while 13% and 4% of the alerted cases were approved after an EPID or ion chamber based phantom check, respectively. The extra time for these phantom measurements amounts to about 30 min per day. This plan was adopted in 68% of the alerts.

**Conclusion:** The automated workflow ensures the timely inspection of each palliative and curative RT treatment at a minimal amount of inspection work. Furthermore, the structured alert handling approach facilitates consistent decision making and is an excellent tool to check the overall clinical process.

Add this talk to vcal | ical | Contact Email: b.mijnheer@nk.nl

- Analysis of alerts during routine in vivo dosimetry with EPIDs
- In vivo reports created post-treatment delivery
- 20 alerts/day were analyzed
- 83% of deviations explained immediately after treatment
- 13% explained with EPID based phantom check
- 4% explained with ion chamber based phantom check
Future Direction

Warning system – critical structure in high dose region

⇒ Intervention: Beam off

Prostate as an example or other OAR

Treatment Field

Probe Detectors
### Phantom Results

Comparison between institution’s plan and delivered dose.

<table>
<thead>
<tr>
<th>Phantom</th>
<th>H&amp;N</th>
<th>Liver insert</th>
<th>Lung</th>
<th>Prostate</th>
<th>Spine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irradiations</td>
<td>1880</td>
<td>143</td>
<td>950</td>
<td>556</td>
<td>308</td>
</tr>
<tr>
<td>Pass</td>
<td>1595 (85%)</td>
<td>105 (73%)</td>
<td>784 (82%)</td>
<td>474 (85%)</td>
<td>237 (77%)</td>
</tr>
<tr>
<td>Fail</td>
<td>285</td>
<td>38</td>
<td>166</td>
<td>82</td>
<td>71</td>
</tr>
<tr>
<td>Criteria</td>
<td>7%/4mm</td>
<td>7%/4mm</td>
<td>5%/5mm</td>
<td>7%/4mm</td>
<td>5%/3mm</td>
</tr>
</tbody>
</table>

Global Leaders in Clinical Trial Quality Assurance

Courtesy of David Followill
Conclusion

• In vivo dosimetry is needed:

  (143) Many of the accidents described in this publication could have been avoided if in-vivo measurements had been performed on a selected group of patients. In-vivo measurements (Leuven et al., 1990; Garavaglia et al., 1993; Van Dam and Marinello, 1994) are an effective way of verifying the quality of the entire radiotherapy treatment procedure. The additional cost of in-vivo dosimetry does not require a considerable increase in funding even in a small hospital (Kesteloot et al., 1993). It is an especially valuable investment, but to be effective, it requires careful preparation in terms of equipment, staff training and quality assurance.

  (144) Diodes and thermoluminescent dosimeters can be used for in-vivo measurements. It is important to realise that when the detector used for in-vivo dosimetry has been calibrated in the same treatment unit where patients are treated, the results from in-vivo measurements will be correlated with the calibration of the machine and, therefore, will not be able to show a potential error in the calibration of the machine. A correct calibration of the dosimeter is thus an essential necessity.

• Developments of in vivo dosimetry technology must target

  – Real-time feedback and algorithms that identifies error types and facilitate decision making
  – Compatibility with workflow (e.g. straightforward calibration)
  – Software that facilitates straightforward operation of technology
The role of In Vivo Dosimetry

**SHOULD**

no longer be ignored