Evolution of brachytherapy in providing conformal plans – from 2D to 3D IGABT, IPSA and HIPO

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Disclosures & Acknowledgements

• Teaching Faculty for the ESTRO GYN TCs (2016 onwards).

• Certified International trainer for Gyn Brachy by Eckert and Ziegler Bebig GmbH.

• Co-author: IBS Guidelines for Cervical Cancer and Member Co-ordination Committee of AROI for AROI ESTRO Gyn TCs.

• Teaching material from GYN GEC ESTRO Teaching Courses (2012 – 2020).

• Prof. Richard Poetter, Prof. Kari Tanderup, Prof. Christine Haie Meder, Prof. Umesh Mahantshetty and Prof. Jamema Swamidas.

• Present and previous faculty members, residents, nursing personnel and staff at The Departments of Radiation Oncology, RGKMCH, Kolkata and BMCH, Burdwan.
BRACHYTHERAPY : WHAT?
EBRT vs BT
Advantages of BT

• Conforms to irregular tumor volumes.
• Avoids geographical misses - moves with the tumor.
• Rapid dose fall off.
• Center of tumor (hypoxic / radio-resistant area) actually receives much higher dose.

Adapted from Nag, S.
BRACHYTHERAPY IN CARCINOMA CERVIX : WHY?
Advantages of BT : Eg : Cervix
Advantages of BT: Eg: Cervix
BRACHYTHERAPY : EVOLUTION
Journey from 2D to 3D
Journey from 2D to 3D

- Imaging
- Applicators
- Dosimetry
BRACHYTHERAPY : EVOLUTION IMAGING
2D Orthogonal X-ray based concept
Assessment modalities

<table>
<thead>
<tr>
<th></th>
<th>Clinical</th>
<th>USG</th>
<th>CT</th>
<th>MRI</th>
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<tbody>
<tr>
<td>Availability</td>
<td>Gold</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td>Gold</td>
<td>Silver+</td>
<td>Silver</td>
<td>Gold</td>
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</tbody>
</table>

Pre EBRT Correlation (Pearson’s correlation coefficients)

<table>
<thead>
<tr>
<th></th>
<th>MRI-CLINICAL</th>
<th>MRI-USG</th>
<th>MRI-CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antero-Posterior</td>
<td>0.48</td>
<td>0.49</td>
<td>0.73</td>
</tr>
<tr>
<td>Medio-Lateral</td>
<td>0.18</td>
<td>0.14</td>
<td>0.62</td>
</tr>
<tr>
<td>Supero-Inferior</td>
<td>0.23</td>
<td>0.45</td>
<td>0.66</td>
</tr>
</tbody>
</table>
Journey from 2D to 3D
The GYN GEC ESTRO I – IV recommendations

Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV

Christine Haie-Meder, Richard Pötter, Erik Van Limbergen, Edith Briot,

Recommendations from gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy—3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology

Richard Pötter, Christine Haie-Meder, Erik Van Limbergen, Isabelle Barillot,

Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group: Considerations and pitfalls in commissioning and applicator reconstruction in 3D image-based treatment planning of cervix cancer brachytherapy

Taran Paulsen Hellebust, Christian Kirisits, Daniel Berger, José Pérez-Calatayud,

Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (IV): Basic principles and parameters for MR imaging within the frame of image based adaptive cervix cancer brachytherapy

Johannes C.A. Dimopoulos, Peter Petrow, Kari Tanderup, Primož Petrič, Daniel Berger,
Journey from 2D to 3D
The Indian Brachytherapy Society recommendations

Indian Brachytherapy Society Guidelines for radiotherapeutic management of cervical cancer with special emphasis on high-dose-rate brachytherapy

Umesh Mahantshetty, MD¹, Shivakumar Gudi, MD¹, Roshni Singh, MD¹, Ajay Sasidharan, MD¹, Supriya (Chopra) Sastri, MD¹, Lavanya Gurram, MD¹, Dayanand Sharma, MD², Selvaluxmy Ganeshrajah, MD³, Janaki MG, MD⁴, Dinesh Badakh, MD⁵, Abhishek Basu, MD⁶, Francis James, MD⁷, Jamema V Swamidas, PhD³, Thayalan Kuppuswamy, PhD⁹, Rajendra Bhalavat, MD¹⁰

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MRI protocol

- T2w FSE sequences
- Vaginal jelly
- Para images

Table 1

Image acquisition protocols for pre-RT MRI scan and BT MRI scan. This table summarizes the important information regarding sequence, plane orientation, coverage/borders for each of the different MRI sequences.

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Number</th>
<th>Mandatory (M)/optional (O)</th>
<th>Sequence</th>
<th>Plane orientation</th>
<th>Coverage/borders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-RT MRI scan</td>
<td>1</td>
<td>M</td>
<td>T1 FSE</td>
<td>Para-axial (according to cervix uteri)</td>
<td>Above uterine corpus – inferior border of symphysis pubis/entire vagina if distal vaginal involvement</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>M</td>
<td>T2 FSE</td>
<td>Sagittal</td>
<td>Pelvic side wall (obturato muscle)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>M</td>
<td>T2 FSE</td>
<td>Para-coronal (according to cervix uteri)</td>
<td>Uterine corpus – cervix – vagina – tumour</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>M</td>
<td>T2 FSE</td>
<td>Axial</td>
<td>Discus 14-15 – inferior border of symphysis pubis/entire vagina and inginal regions if distal vaginal involvement</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>O</td>
<td>T1 FSE or 3D GRE without contrast</td>
<td>Axial</td>
<td>Discus 14-15 – inferior border of symphysis pubis/entire vagina and inginal regions if distal vaginal involvement</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>O</td>
<td>T1 FSE with contrast</td>
<td>Sagittal</td>
<td>Pelvic side wall (obturato muscle)</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>O</td>
<td>T1 FSE or 3D GRE with contrast</td>
<td>Axial (isotropic 3D GRE)</td>
<td>Uterine corpus – cervix – vagina – tumour</td>
</tr>
<tr>
<td>BT MRI scan</td>
<td>8</td>
<td>M</td>
<td>T2 FSE</td>
<td>Para-axial (according to cervix uteri)</td>
<td>Above uterine corpus – 3 cm below lower surface of vaginal applicator/entire vagina if distal vaginal involvement</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>M</td>
<td>T2 FSE</td>
<td>Para-sagittal (according to cervix uteri)</td>
<td>Pelvic side wall (obturato muscle)</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>M</td>
<td>T2 FSE</td>
<td>Para-coronal (according to cervix uteri)</td>
<td>Uterine corpus – cervix – vagina – tumour</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>O</td>
<td>T2 FSE</td>
<td>Axial</td>
<td>Above uterine corpus – 3 cm below lower surface of vaginal applicator/entire vagina if distal vaginal involvement</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>O</td>
<td>3D T2 FSE isotropic</td>
<td>Coronal or axial with reconstructions</td>
<td>Large coverage inherent in this sequence</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>O</td>
<td>T1 FSE, FLASH, T1 GRE 3D</td>
<td>As appropriate</td>
<td>At least entire applicator</td>
</tr>
</tbody>
</table>

*When contrast series are applied (6 and/or 7): use same T1 sequence for pre-contrast and lymph node evaluation.*
### Different 3D environments

<table>
<thead>
<tr>
<th>Environments</th>
<th>At diagnosis</th>
<th>Before Brachytherapy</th>
<th>At Brachytherapy</th>
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</thead>
<tbody>
<tr>
<td>MR – MR</td>
<td>MR + Clinical</td>
<td>Clinical ± MR</td>
<td>MR* + Clinical</td>
</tr>
<tr>
<td>MR – CT</td>
<td>MR + Clinical</td>
<td>MR + Clinical</td>
<td>CT* + Clinical</td>
</tr>
<tr>
<td>CT – CT</td>
<td>CT + Clinical</td>
<td>Clinical ± CT</td>
<td>CT + Clinical</td>
</tr>
</tbody>
</table>

* - at least for the first fraction
CT Imaging protocol

- Bladder filling with dilute contrast.
- IV contrast – arterial phase – blush!
- Axial 2-3 mm slices.
- MR compatible applicators.
CT based target delineation

Original Article

IBS-GEC ESTRO-ABS recommendations for CT based contouring in image guided adaptive brachytherapy for cervical cancer

Umesh Mahantshetty a,*, Richard Poetter b,*, Sushil Beriwal c, Surbhi Grover d, Gurram Lavanya e, Bhavana Rai f, Primož Petric g, Kari Tanderup h, Heloisa Carvalho i, Neamat Hegazy k, Sandy Mohamed l, Tatsuya Ohno m, Napapat Amornwichet n

Fig. 2. Schematic diagram showing definition of CTV- TIBC for CTB - CTB Environment based on the disease at diagnosis (cervix and parametrium in blue fill & vaginal disease in green lines), residual disease at BT (blue oblique lines), CTV-TB (in red continuous lines) and safety margins (red dotted lines). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
Journey from 2D to 3D
The Indian Brachytherapy Society recommendations

Indian Brachytherapy Society Guidelines for radiotherapeutic management of cervical cancer with special emphasis on high-dose-rate brachytherapy

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• Mrs. MS, 66 yr, HTN, white discharge with spotting 4 months.

Stage FIGO IIB
- $w = 5 \text{ cm}$
- $h = 4.5 \text{ cm}$
- $t = 3 \text{ cm}$

Vagina: 2.5 cm
10 o clock to 2 o clock

Case MR; Name: MS RT/2190/18
Adaptive MRI based planning: 4D RT

Dimopoulos et al. StrahlOnkol 2008
TRUS Guided Prostate Brachytherapy : 4D
BRACHYTHERAPY : EVOLUTION
TARGET CONCEPTS
The concept of Point A and B

- Lateral throw-off of dose
- Obturator node

- Nodal dose ~ 3Gy for 4
- # of 7 Gy each

20-25% 100%
Modifications of Point A
The ICRU Bladder and Rectal Points
GYN GEC ESTRO concepts

Three different target volumes according to cancer cell density

Pelvic wall region

Potential microscopic tumour spread

Macrosopic tumour load

Potential microscopic tumour spread

LR  IR  HR  IR  LR

Pelvic wall region

Significant microscopic disease

Significant microscopic disease

HR: High risk CTV
IR: Intermediate risk CTV
LR: Low risk CTV

GES ESTRO recommendations 2005
ICRU 89 concepts: CTV

*Initial Tumor Extension at Time of Diagnosis*

- GTV<sub>init</sub> = 90 cm<sup>3</sup>
- CTV-T = 300 cm<sup>3</sup>

*Treatment*

- Patterns of GTV Response
  - **Stable Disease**
    - GTV<sub>res</sub>
      - GTV<sub>res</sub>: V = 90 cm<sup>3</sup>
  - **Partial Remission**
    - GTV<sub>res</sub>
      - GTV<sub>res</sub>: V = 30 cm<sup>3</sup>, Patho. tissue: V = 20 cm<sup>3</sup>
  - **Complete Remission**
    - GTV<sub>res</sub>
      - GTV<sub>res</sub>: V = 0 cm<sup>3</sup>, Patho. tissue: 20 cm<sup>3</sup>
      - GTV<sub>res</sub>: V = 0 cm<sup>3</sup>, (microscopic residual tumor cells)

*Adaptive CTV based on GTV response*

- CTV-adap: V = 300 cm<sup>3</sup>
- CTV-adap: V = 60 cm<sup>3</sup>
- CTV-adap: V = 40 cm<sup>3</sup>
- CTV-adap: V = 30 cm<sup>3</sup>
- CTV-adap: V = 10 cm<sup>3</sup>

*Adaptive Treatment*

- GTV<sub>init</sub>
- CTV-T
- GTV<sub>res</sub>
- CTVadap
- Pathologic tissue

GEC ESTRO II and ICRU 89 Fig. 5.3
Morbidity related anatomical reference points and volumes for important OARs

**Figure 6.4.** Schematic anatomical diagrams (sagittal view) showing two different positions of the vaginal part of the utero-vaginal applicators, the cervix tumor, the uterus, and the reference volumes of OARs in two different patients. The most irradiated-tissue volumes adjacent to the applicator, i.e., the reference volumes 0.1 cm$^3$, 2 cm$^3$, and 5 cm$^3$, are illustrated for the various adjacent organs such as the bladder (neck), rectum (anus), sigmoid, and small bowel (see Section 8.4.1). The two panels show the different locations of the 0.1 cm$^3$ and 2 cm$^3$ reference volumes in the adjacent OARs [modified from GEC ESTRO Recommendations II; see also Westerveld et al. (2013)]. Reference points are indicated for the bladder (ICRU, 1985), the rectum and upper vagina (ICRU, 1985), and the mid- and lower vagina (PIBS ± 2 cm). The vaginal reference length (VRL) (PIBS to midpoint between the vaginal sources) can serve as an indicator to assess the varying position of the vaginal sources relative to the surrounding normal-tissue structures (Westerveld et al., 2013).
BRACHYTHERAPY: EVOLUTION APPLICATORS

The slides in this section are courtesy of Dr. Primoz Petric and Prof. Richard Poetter.
The “systems”

Gosta Forssell
Stockholm System

Claude Regaud
Paris System

M.C. Todd
W.J. Meredith
Manchester System

Edith Quimby
Quimby System

R. Paterson & H.M Parker
Manchester System

B. Pierquin & A. Dutreix
Paris System

Intracavitary systems

Interstitial systems
Historical Paris Technique

1910-1920: Curie Institute, Paris, France

Applicator:
- Rubber tandem
- Cork colpostats (paraffin coated)
- Distance – colpostats: not fixed
- $^{226}\text{Ra}$ preloading
  - $X$ mg of $^{226}\text{Ra}$ for $Y$ hours

Typical application
- $\approx 5$ days ($120 \text{ h}$)
- 7000-8000 mgh

Claude Regaud
Classical Stockholm method

1913-1914: Radiumhemmet, Stockholm, Sweden

Applicator:

- Flat box (plate)
- Flexible tube

Not connected → No fixed geometry

\(^{226}\text{Ra}\) preloading

- \(X\) mg of \(^{226}\text{Ra}\) for \(Y\) hours

Typical treatment

- 2 – 3 applications (≈ 20-30 h)
- \(\approx 7000\) mgh

Gosta Forssell
Historical Manchester System

Related to historical Paris technique

Applicator:
- no fixed geometry
- Intrauterine tube
- Vaginal ovoid
- Flange
- Spacer

Photo: Institute of Oncology Ljubljana

226Ra preloading (mg):
- 3 cm (L): 22.5 mg
- 2.5 cm (M): 20 mg
- 2 cm (S): 17.5 mg

6 cm 10 10 15
4 cm 10 10 15
3.5 cm 20 20 17.5

Given tumour volume

A set of rules
- Geometry
- mg of 226Ra
- Duration

Certain point A dose

Typical treatment:
- 140 hours for 7500 R at point A (dose rate 53 R/h)

Modern Intracavitary Techniques

Applicators: mimicking historical geometries

Manchester / Fletcher style

Common features:

Uterine Tandem: various lengths, angles or curvatures

Ovoids, cylinders, rings: various outer & source path diameters

Clamp

Stockholm style

Source path $\phi$:
- 26 mm
- 30 mm
- 34 mm

Outer $\phi$:
- 38 mm
- 42 mm
- 47 mm
Applicator selection based on tumour topography

Courtesy of Daniel Berger and Primoz Petric
Applicator selection based on tumour topography
Advanced brachytherapy applicators

Courtesy of Daniel Berger and Primoz Petric
BRACHYTHERAPY : EVOLUTION

DOSIMETRY
Optimal geometry

Ideal application
Longest tandem
Largest ovoids
Perfect pear

Poor application
Shorter tandem
Largest ovoids
Flattened pear

Poor application
Longest tandem
Smaller ovoids
Narrowed pear
Optimal geometry

Ideal application and dose distribution

Inappropriate application and resultant dose distributions
Brachytherapy Planning

Golden Rule

Good planning and optimization cannot turn a poor insertion into a great plan!
MRI images
Steps of brachytherapy planning

1. Applicator reconstruction
   Manual, library based

2. Standard loading
   Based on known loading patterns from systems

3. Normalization to a point
   Planning aim vs Prescribed dose

4. Plan Optimization
   Methods
Summation of EBRT and Brachytherapy doses by EQD2
Reporting and auditing

Level 3: Research-oriented reporting
All that is reported in Level 1 and 2 plus

Absorbed-dose reporting for the tumor:
- \( D_{98\%}, D_{90\%} \) for the CTV\(_{IR} \) even if not used for prescription
- \( D_{90\%} \) for the GTV\(_{res} \)
- DVH parameters for the PTV
- \( D_{50\%} \) for pathological lymph nodes
- DVH parameters for non-involved nodes (ext/int iliac, common iliac)

OAR volumes and points
- Additional bladder and rectum reference points
- OAR sub-volumes (e.g., trigonum or bladder neck, sphincter muscles)
- Vagina (upper, middle, lower)
- Anal canal (sphincter)
- Vulva (labia, clitoris)
- Other volumes/sub-volumes of interest (e.g., ureter)

Dose–volume reporting for OARs
- Dose–volume and DSH parameters for additional OARs and sub-volumes
- Vaginal dose profiles, dose–volume, and DSHs
- Length of treated vagina

Isodose surface volumes
- 85 Gy EQD2 volume
- 60 Gy EQD2 volume
BRACHYTHERAPY : EVOLUTION OPTIMIZATION
Optimization

• Design a distribution of source terms such that the resultant dose distribution satisfies certain constraints and meets certain objectives as well as possible.

1. Forward Optimization (FO)
   – Dwell time – adjust dwell times at each source position
   – Geometric – based on implant geometry
   – Graphical – local vs global; drag isodoses

2. Inverse Optimization (IO)
   - IPSA
   - HIPO
Brachy Optimization Types

- **Forward** – tedious but more robust.
  - Generate plan
  - Define objectives
  - Optimize plan

- **Inverse** – fast but less robust.
  - Define objectives
  - Optimize plan
  - Generate plan
Inverse planning is only relevant when numerous applicators (needles, catheters are used and the planning process by Forward Planning Optimization is complex, laborious and time consuming).
Simulated Annealing

• Simulated annealing (SA) is a probabilistic technique for approximating the global optimum of a given cost function.
• Specifically, it is a metaheuristic to approximate global optimization in a large search space for an optimization problem. The technique used is Stochastic Optimization.
• For problems where finding an approximate global optimum is more important than finding a precise local optimum in a fixed amount of time, simulated annealing may be preferable.
• The name of the algorithm comes from annealing in metallurgy (a technique involving heating and controlled cooling of a material to alter its physical properties).
Inverse Planning Simulated Annealing

- CT-based inverse planning.
- Produce an optimized plan in a very short time.
- Uses stochastic optimization only.
- Used for prostate (permanent implants, HDR), breast.

- Dose coverage of PTV (V100) lower.
- Dose homogeneity Index lower.
- Overloading of needle ends, higher active length, redundant dwell positions.
- DVH parameters often suboptimal.
Hybrid Inverse Planning Optimization

- CT-based inverse planning.
- Produce an optimized plan in a very short time.
- Uses both stochastic and deterministic optimization.
- Used for prostate, breast, gynaecological implants.

- Dose coverage of PTV (V100) higher.
- Dose homogeneity Index higher.
- Overloading of needle ends, higher active length, redundant dwell positions.
- DVH parameters better and comparable to FO.
Dosimetric comparison of inverse optimisation methods versus forward optimisation in HDR brachytherapy of breast, cervical and prostate cancer

Georgina Fröhlich, Gyula Geszti, Júlia Vízkeleti, Péter Ágoston, Csaba Polgár, Tibor Major

Fig. 1 Dose distributions using HIPO (hybrid inverse planning optimisation), IPSA (inverse planning simulated annealing) and forward optimisation (FO) in interstitial BT (brachytherapy) of breast (a), cervical (b) and prostate (c) cancer. Red dots: active dwell positions (volumes: red: PTV [planning target volume]; a green: non-target breast, blue: ipsilateral lung, pink: ribs; b yellow: bladder, green: rectum, violet: sigmoid, pink: vagina; c yellow: urethra, green: rectum)

Fig. 2 The absolute volume irradiated by 100% of the prescribed dose ($V_{100}$) using HIPO (hybrid inverse planning optimisation), IPSA (inverse planning simulated annealing) and forward optimisation (FO) methods in interstitial cervical BT (brachytherapy) plans.
**Conclusions**

For image-guided cervix cancer treatments, both IMRT and IMPT seem to be inferior to BT.
Thank You

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