ICRU 89: Time to move beyond point A?- Update in CT adaptation for brachytherapy

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Conflict of Interest

I have two pending IP rights on CT compatible Intravaginal templates for use in treatment of cervix cancer brachytherapy by IGABT.
We will discuss.

Evolution of Volume based IGBT.
Relevant points of ICRU 89.
Relation between point based and volume based planning.
Problems of IGABT(MRI).
Advantages/ disadvantages of CT guided BT.
CT guided IGABT guidelines.
Clinical results of CT guided BT.
Implementing CT guided IGABT in clinical practice.
Margaret Cleves first used Radium in treatment of cervix cancer.

**Stockholm System** - IC brachytherapy Started in 1910.

**Paris System** – ICBT started at Paris

**Manchester system**
Todd and Meridith in 1930 -- Point based system and prescription rules. Concept of OARs

- Point Based ICRT ruled the arena for more than 70 years.
- Excellent control rates of cancer cervix in combination with EBRT and CCT.
- A technique of boast for Radiation oncologist offering unparallel cure rates compared to any other disease in the contemporary times.
Evolution of imaging in brachytherapy and the corresponding literature

Plain x ray
International standard until 2002

2002-2011, more and more centers started using CT based planning

Started around 1998, Multiple reports published By 2010.

Numerous research articles.

Clinical results available from 2000 till date.
ESTRo/ABS/IBS Guidelines in 2021

GEC ESTRO group 2000.
Recommendations –2005-2012
Clinical Outcome results 2017/2021/
ICRU 89 - 2016
Why a need was felt to replace point A?

Talks to replace Point A did not happened because of its inherent criticisms!

- Not being a true anatomical point.
- Not reproducible in all fractions.
- Does not represents true tumour volume.
- Confusions about its true positions.
- Lack of correlation of dose and outcomes.

Rather we attained new advancements and have new needs.

- Volumetric imaging at diagnosis and Brachytherapy.
- Compatible applicators.
- Understanding the contouring of target volumes.
- Better optimisation of treatment plans in volumetric planning.
- Advent of IC+IS techniques that mandates volumetric imaging and volume delineations.
- In pouring clinical results showing more control and less toxicities with IGBT.
Volumetric images – Point A dose prescription is inadequate

Left/Rt - maximum width 2 cm.
The Point A dose is representative of CTVHR

- Maximum width of 4 cm Rt side.
- 45 Gy EBRT+ 7GyX4 HDR.
- Right EQD2 to 57 Gy (47%)

- Dmax HRCTV 2.5 cm
- Left EQD2 78 Gy EQD2 78 Gy (80%)
IC+IS technique of Brachytherapy and IGABT

• In todays radiotherapy you treat only after U see.
• Complex IC/IS techniques are not performed without imaging.
• A better method than Point A replacement can be discussed.
IGABT and IC+IS BT are complimentary for better LC in advanced Ca Cervix

- Actuarial 3 years LC is shown for each box.
- For dose escalation and de-escalation two things are necessary: IGABT, IC+IS/IS brachytherapy.

Dose de-escalation

<30 cm³, No higher local control

Dose escalation

>30 cc,
Receiving less than 85 Gy so poor LC

Distribution of CTVHR dose and volume in the EMBRACE study
No Brachytherapy Vs 2D/3D Brachytherapy

Brachy boost compared to IMRT boost and 2D boost

Total 25% improvement in OS

GEC ESTRO teaching course slide
ICRU 89 on basis of GECESTRO guidelines validated by Retro embrace and EMBRACE trials.

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

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

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

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
Prescribing, Recording, and Reporting Brachytherapy for Cancer of the Cervix

Sections 1-12
Summary (end of each section)
Key messages (1-4, 9, 12)
Recommendations (5-8, 10-11)

Chapter (1) – Introduction
Chapter (2) – Prevention, Diagnosis, Prognosis, Treatment and Outcome
Chapter (3) – Brachytherapy Techniques and Systems
Chapter (4) – Brachytherapy Imaging for Treatment Planning
Chapter (5) – Tumor and Target Volumes and Adaptive Radiotherapy
Chapter (6) – Organs At Risk and Morbidity-Related Concepts and Volumes
Chapter (7) – Radiobiological considerations
Chapter (8) – Dose and Volume Parameters for Prescribing, Recording, and Reporting Brachytherapy, Alone or combined with External Beam Therapy
Chapter (9) – Volumetric Dose Assessment
Chapter (10) – Radiographic Dose Assessment
Chapter (11) – Sources and Absorbed-Dose Calculation
Chapter (12) – Treatment planning
Chapter (13) – Summary of The Recommendations

Appendix A: 9 Comprehensive Clinical Examples (various clinical/technical scenarios)
ICRU 89 Adaptive IGBT

- Emphasizes adaptive, 4D (3D and time) treatment approach.
- Improve the efficacy/toxicity ratio by exploiting the tumor-volume regression
• Initial GTV plus margins.
• Initial GTV alone
• Initial sub-GTVs

• Residual GTV + residual pathologic tissue in the area of the initial GTV + tumor-bearing organ
• Res GTV plus residual pathologic tissue in the area of the initial GTV.
• Residual GTV alone plus margins
• Residual GTV alone.
• Residual sub-GTVs.
Target volume concepts

High Risk CTV:
GTV at time of brachytherapy
In all cases includes:
GTV + whole cervix
  Presumed tumour extension in adjacent tissues Clinical assessment
  Residual grey zones on MRI

NO SAFETY MARGINS

Intermediate Risk CTV:
GTV at time of diagnosis
In all cases includes:
HR-CTV
Integrates initial GTV

SAFETY MARGINS
Concept of adaptive concept as per ICRU89

GTV Res + Cervix+ Grey Zones (in region of previous GTV) = HRCTV

Initial GTV + HRCTV  Cervix + Margin = IRCTV

CTVLR = Treated during EBRT
• The GEC ESTRO - 10 mm margin in the Lat and CC directions and 5 mm AP direction.
• Margin at the borders of the CTV-THR where there was no initial GTV-T.
• Stable disease, CTV-THR becomes similar to the GTV-T init, with margins for IRCTV.
• In the case of rectal/bladder invasion, CTV-T margins should not go into the organ lumen
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.

- BT-related morbidity are usually linked to small volumes receiving high absorbed doses.
- For small OAR planning and reporting (0.1 or 2 cm³ it is sufficient to delineate one outer contour.
- Telangiectasia, ulceration, necrosis, or fistula dose to 0.1 or 2 cc.
• USG may become essential— even competitive with MRI.
• The adaptive volumetric CTV-THR concept can be applied on CT images and clinical examination are available for treatment planning.
• GTV-Tres can only be defined based on the clinical examination.
• Height of HRCTV cannot be assessed from CT images or clinical examination.
• Can be followed in Radiograph with limited accuracy.
You can’t move forward until you look back.

Cornel West
Relationship between point A/HRCTV/IRCTV

- The Point-A absorbed dose cannot predict the target absorbed dose in individual patients.
- It provides a reasonable estimate of the average CTVHR D90 % for a population with a balanced disease-stage Distribution.
- It is possible to proceed from the average dose prescription at Point A to the average dose prescribed to the CTVHR.
- The treatment to the 60 Gy isodose line approximately the CTVIR.
The data exhibit a largely linear relationship but with a sizable variation for individual patients (EMBRACE, 2015)
Clinical relevance of the bladder and rectal reference points

- ICRU Rectal point doses - not a good predictor of D2cm3 in the individual patient.
- 20% larger with (SD 40%)
- ICRU bladder dose - is almost 20% smaller than bladder D2cm3 (SD 32%).
- ICRU rectal point has clinical correlation.
- Bladder reference point no clinical correlation proved.
<table>
<thead>
<tr>
<th>Target Volumes</th>
<th>OAR delineation</th>
<th>Treatment Planning</th>
<th>Ease of access</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical examination under sedation <strong>and Documentation</strong></td>
<td>Vaginal (both OAR and Target) extent of disease.</td>
<td>NA</td>
<td>Available</td>
</tr>
<tr>
<td>MR</td>
<td>Gold standard</td>
<td>Very accurate</td>
<td>Difficult outside clinical trial.</td>
</tr>
<tr>
<td>CT</td>
<td>Needs supplementary information.</td>
<td>Accurate</td>
<td>Easily available.</td>
</tr>
<tr>
<td>USG</td>
<td>Comparable to MRI (Training required)</td>
<td>Not encouraged.</td>
<td>Not practised in India</td>
</tr>
</tbody>
</table>

**Gold Standard**

**Very accurate**

**More training than CT based Planning required**

**Wide availability**

**Can be made easily available.**
Patterns of cervical cancer brachytherapy in India: results of an online survey supported by the Indian Brachytherapy Society

Abhishek Chattopadhyay, MD; Subhash Grover, MD; MPH; Lavanya Gwiram, MD; Prof. Supriya Sosti, MD; Prof. Umesh Mohanty, MD

centers in more than 30% of cases. Some form of imaging was performed for planning by 97% (57/59 centers) of respondents, with CT scan (65%, 38/59 centers) and

Image verification

G. Suneja et al. / Brachytherapy 2016

3% No
23% X-ray
3% Ultrasound
64% CT
10% MRI
Contouring of normal organs in IGABT

- MR represents better resolution even for normal organ contouring.
- Contouring or outer wall only is recommended.
- Whole lumen contouring makes CT contouring comparable with MR.
- Bladder is a complex organ to contour.
The contouring methods didn’t tool other complimentary imaging like USG in view.

• No contrast used in CT scan.

• A more meticulous mapping may improve the HRCTV drawn on CT.

• A must read paper to understand the message delivered.
MR VS CT based IGABT

• Gold standard in delineation.
• Experience widely published in last 15 years.
• Clinical results are excellent both in tumour control and toxicity.
• Standard guidelines, Validated by Multicentric study.

• Not available in most centres for BT.
• MR compatible applicators are considered fragile and costly.
• Applicator reconstruction needs expertise.
• The benefits of IGABT specially IC+IS techniques cant reach where needed most.

• Commonly available in most department even in developing countries.
• Considered more user and pocket friendly.
• Literature is adding up.
• Time to disseminate benefits of IGABT by use of CT

• Complementary findings and imaging.
• Easily available.
• Easy applicator and catheter recon.
• Results of MR-IGABT yet to be replicated.
Conventional ICRT vs IGBT

2D
- Cheap and cost effective
- Treatment of mass
- Time tested
- Unpredictable toxicity.
- I just love my first Bike.

4D-CT IGBT
- More Safe.
- Affordable and cost effective
- Costly than Bike on initial investment,
- Better for long drive (bigger tumors)
- Less late toxicity.
- NO GPS(Printed Map and asking others).

4D-MRIGBT
- Real time GPS to reach destination(HRCTV Dose).
- Back Camera (More visible OARs).
- Costly/ Not all can afford.
Recognising CT as standard volumetric imaging modality

CT can be used for planning as an alternative to MRI.

CT for delineation of organs at risk and evaluation of volume histogram parameters is routine.

Tumor-related target area of current research.

The use of CT imaging for treatment planning is...
Complementary clinical and imaging

- 35 patients.
- Information of comprehensive 3D documentation of repetitive gynecological examination in the HRCTV of CT.
- Use of 3D clinical drawings, significantly improves the HRCTV volume and width estimation.

- 25 patients
- Use of Clinical exam, MRI at diagnosis and TRUS at BT.
- The mean differences in HR-CTV width between CTandMRI contours at various levels, only 0.1 to 0.4 cm.
- Almost like Gold standard.
Quantitative documentation of Clinical examinations- an essential adjunct for CTIGABT.

**IBS guidelines**

- NMD
- Incorporating Radiological information.
- Width of the disease.
The need of CT based contouring was acknowledged and multiple Guidelines are in place.
No parametrial extension - **Identical HCTV (MR/CT).**

Parametrial extension & poor response - **Identical HCTV (MR/CT).**

Parametrial extension with a CR - **More difference in HRCTV.**

MRI volumes are smaller than CT.

CT volumes - higher level of agreement.

Safety Margin for height.

Uncertainty of lateral borders

Recognising inputs from ancillary findings
### Categorisation of response – for drawing HRCTV in CT

<table>
<thead>
<tr>
<th>Category of BT</th>
<th>Cervix</th>
<th>Parametrium</th>
<th>Vagina</th>
<th>Uterine corpus</th>
<th>bladder/rectum</th>
</tr>
</thead>
<tbody>
<tr>
<td>I&lt;sub&gt;BT&lt;/sub&gt;</td>
<td>No residual disease Or Residual disease confined to cervix</td>
<td>No residual disease</td>
<td>No residual disease Or Residual disease &lt; 2 cm of upper vagina</td>
<td>No residual disease Or Residual disease in proximal third of utero-cervical junction</td>
<td>No residual wall/mucosa involvement</td>
</tr>
<tr>
<td>II&lt;sub&gt;BT&lt;/sub&gt;</td>
<td>Significant residual disease</td>
<td>Proximal parametrial disease</td>
<td>Residual disease within upper one third</td>
<td>Residual disease not beyond mid corpus</td>
<td>No residual wall/mucosa involvement</td>
</tr>
<tr>
<td>III&lt;sub&gt;BT&lt;/sub&gt;</td>
<td>Significant residual disease</td>
<td>Distal/upto pelvic wall parametrial disease</td>
<td>Residual disease in mid or lower third</td>
<td>Residual disease into distal corpus/Up to fundus</td>
<td>No residual wall/mucosa involvement</td>
</tr>
<tr>
<td>IV&lt;sub&gt;BT&lt;/sub&gt;</td>
<td>Any residual disease</td>
<td>Proximal parametrial disease</td>
<td>Residual disease within upper one third</td>
<td>Residual disease not beyond mid corpus</td>
<td>Residual disease involving neighboring organ wall/ mucosa (bladder/ rectum)</td>
</tr>
</tbody>
</table>

- Categorisation by response assessment.
- GTV cannot be drawn unless confined to cervix.
- Concept of NMD.
- Meticulous mapping of disease (CE/Vol imaging).
- CT imaging protocol....
- Concept of safety margin in HRCTV
CT – CT

- Include Lower 2/3 of Uterocervical dimension.
- Lateral uncertainty Margin.
- 2 cm circumferential margin for vaginal extn.

MR – CT

- Pre EBRT Height to consider.
- Uncertainty margin laterally.
CT – MR+CT
- Include Lower 2/3 rd of Uterocervical dimension.
- 2 cm circumferential margin for vaginal extn.

MR – MR+CT
- Pre EBRT Height to consider.
What happens to 30 percent centres doing X ray based planning?

• X Ray planning is still the minimum standard required in all guidelines and ICRU89.

• 2.5D planning with clinicians effort.

• Treatment of patients should not be delayed by referring patients if only X ray facilities are available unless the disease is sure to be missed.

• A meticulous 2D treatment conducted at right time may be a clinical preference rather that waiting for a 3 D planning.
Treatment of cervix cancer 3 factors

OTT

Cure

HRCTV Volume

Dose EQD2
Point A based planning - current status

- Point A based/2 D planning is effective.
- Volume of HRCTV, OTT, HRCTVD90-98, Clinicians judgement
Comparing CT and MR based planning, clinical results

- 29 MR, 27 CT patients
- MFU 19.7 months (MR) and 18.4 months (CT)
- 2-year LC MR CT treatments were 96% and 87% (p=0.65).
- Inconclusive due to arms differently chosen/less patients.
## Contemporary reports on CT guided IGABT

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient/Stage</th>
<th>Prescription</th>
<th>tech</th>
<th>Dose</th>
<th>Results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anish et al 2021</td>
<td>53 IIA/IIB</td>
<td>Point A</td>
<td>IC</td>
<td>50 Gy + &amp;GyX3 Fr</td>
<td>75% LV at 3 years</td>
<td>HR-CTV D90 EQD2 79.75 Gy</td>
</tr>
<tr>
<td>Kawashima 2018</td>
<td>84 (Stages IB-IVA)</td>
<td>PointA/HRCTV(optimisation)</td>
<td>IC</td>
<td>40 Gy +CS</td>
<td>3-yr LC 89%</td>
<td>Mean EQD2 for HR-CTV D90 was 73.4 Gy,</td>
</tr>
<tr>
<td>Murakami 2014</td>
<td>51 (Stages IB-IVA)</td>
<td>Point A</td>
<td>IC</td>
<td>40 Gy +CS 2–5 times of 6 Gy HDR-ICBT</td>
<td>3 yr LC rate 91.7%</td>
<td>D90 for HR-CTV was 60</td>
</tr>
<tr>
<td>Kusuda 2018</td>
<td>68 IB1-IVA</td>
<td>Point A</td>
<td>IC</td>
<td>40 Gy +CSHDR18 Gy in 3</td>
<td>2 yr 92 %</td>
<td>HR-CTV D90 &gt;60 Gy</td>
</tr>
</tbody>
</table>
3D IGBT for locally advanced cervical cancer is a more cost-effective option compared with 2D brachytherapy.

Improved outcomes resulting from MR-IGBT have a potential to translate into large macroeconomic gains for the nation even after meeting all expenditures.

Finally, GBT is cost-effective & economically rewarding to patient & society.
Thumb rule of Contouring in CT

- Minimum requirements are clinical examination & documentation, CT or MR imaging at diagnosis
- CT imaging with the applicator in place during BT
- Width – MR Gold standard/ Complimentary information must.
- Height - add for uncertainties/Pre EBRT height.
- Thickness – Cervical thickness/ only rectal/bladder wall for IVA.

(HRCTVMR will get more dose than HRCTVCT)
Medanata AOLO a CT compatible applicator for advanced cancer Cervix BT

The Medanta AOLO template for locally advanced cancer cervix brachytherapy: design and clinical implementation

Sesovan Banerjee, MD, Venkatesan Kaliyaperumal, MSC, Tejinder Kataria, MD, DNB, Dayanithi Kamaraj, MSC
Division of Radiation Oncology, Medanta - The Medicity, Gurgaon, Haryana, India

Table 1. Results of two clinical applications

<table>
<thead>
<tr>
<th></th>
<th>HRCTV volume (cc)</th>
<th>Bladder 2 cc</th>
<th>Rectum 2 cc</th>
<th>Sigmoid 2 cc</th>
<th>HRCTV V90</th>
<th>COIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application 1</td>
<td>55 cc</td>
<td>11.0 Gy</td>
<td>9.36 Gy</td>
<td>8.6 Gy</td>
<td>97%</td>
<td>0.79</td>
</tr>
<tr>
<td>Application 2</td>
<td>54 cc</td>
<td>11.4 Gy</td>
<td>8.96 Gy</td>
<td>8.5 Gy</td>
<td>96%</td>
<td>0.84</td>
</tr>
<tr>
<td>EQD2 (Gy)</td>
<td>75</td>
<td>80.9</td>
<td>74.3</td>
<td>72.24</td>
<td>75</td>
<td>NA</td>
</tr>
<tr>
<td>(EBRT + brachytherapy)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

EBRT = external beam radiotherapy; cc = cubic centimeter; EQD2 = 2 Gy equivalent dose; a/b for rectum, bladder, and sigmoid is 3, for HRCTV is 10, CON = conformal index = PTV/PTV + PTVPD/VPD; PTVPD = PTV receiving prescription dose; VPD = target volume receiving prescription dose; VPTV = volume of PTV.
Results

- 12 patients of advanced cancer cervix FIGO stage II B-IIIC; mean age was 61 years (Range 46-71).

- A HDR dose of 24-28 Gy in 4 fractions was planned. Mean HRCTV volume was 90 cc (range: 58-120 cc).

- The mean EQD2 (considering alpha/beta=10) of D90 and D98 for HRCTV was 93 Gy and 80 Gy respectively.

- Mean EQD2 of 2 cc rectum and bladder was 79 Gy and 86 Gy respectively.

- All patients had complete clinical and radiological response with no >Grade 2 toxicity.
The details of applicators and its validation have been published and presented in national and internal platform.
Summary

• Point A based Brachytherapy has been backbone of cervix brachy.
• Point based and Volume based brachytherapy have correlations but with unacceptable standard deviation.
• ICRU 89 explains concepts of Volumetric and image guided brachytherapy for cancer cervix.
• MRI is the gold standard of IGABT.
• Complementary imaging, clinical examination and documentation can improve HRCTV volumes considerably.
• IC+IS Brachytherapy does not allow us to continue prescription to point A.
• 2D brachytherapy is not obsolete.
Take home message

Some training and experience is required.
Thank them - that we are here