

# BrachyNext



Working Together to Shape the Future of  
**Brachytherapy**

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**Brachytherapy**

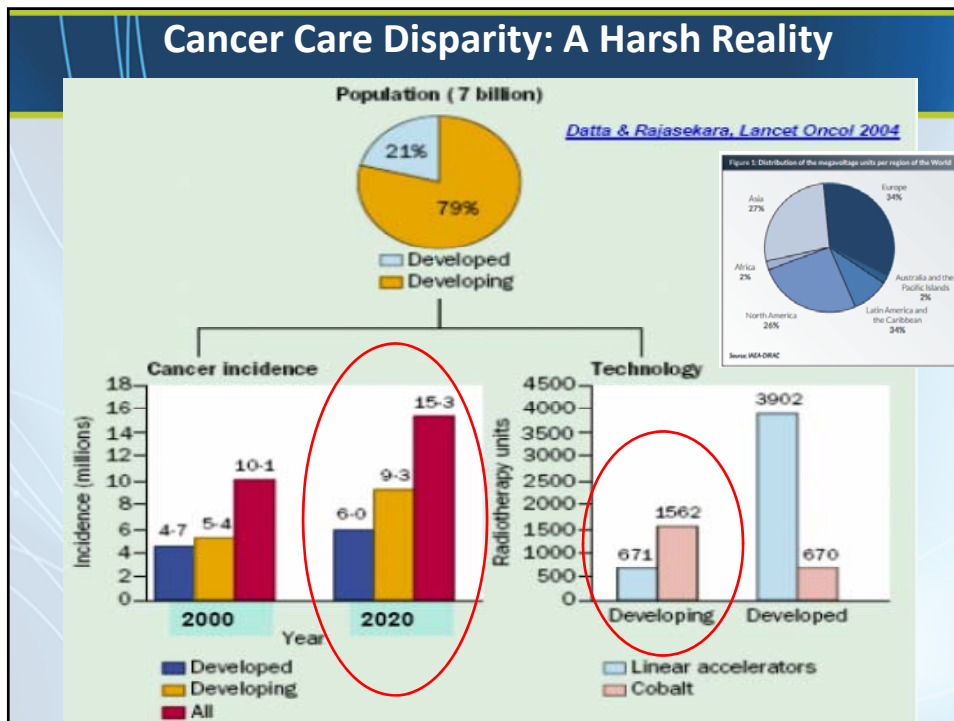
## **Implementation in Clinical Practice: Challenges in Developing Economies**

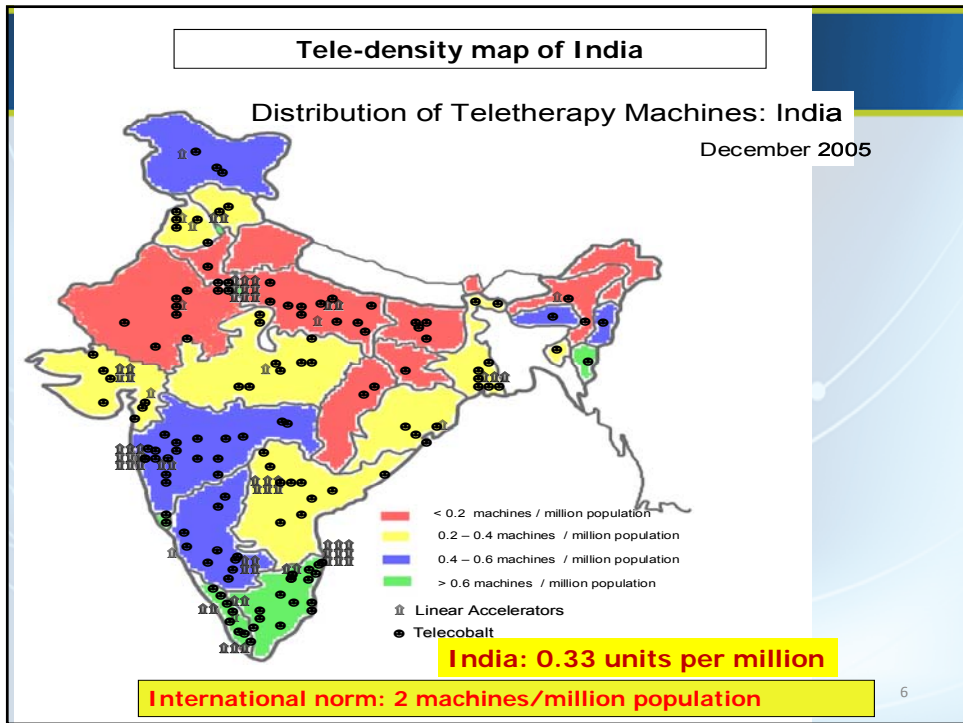
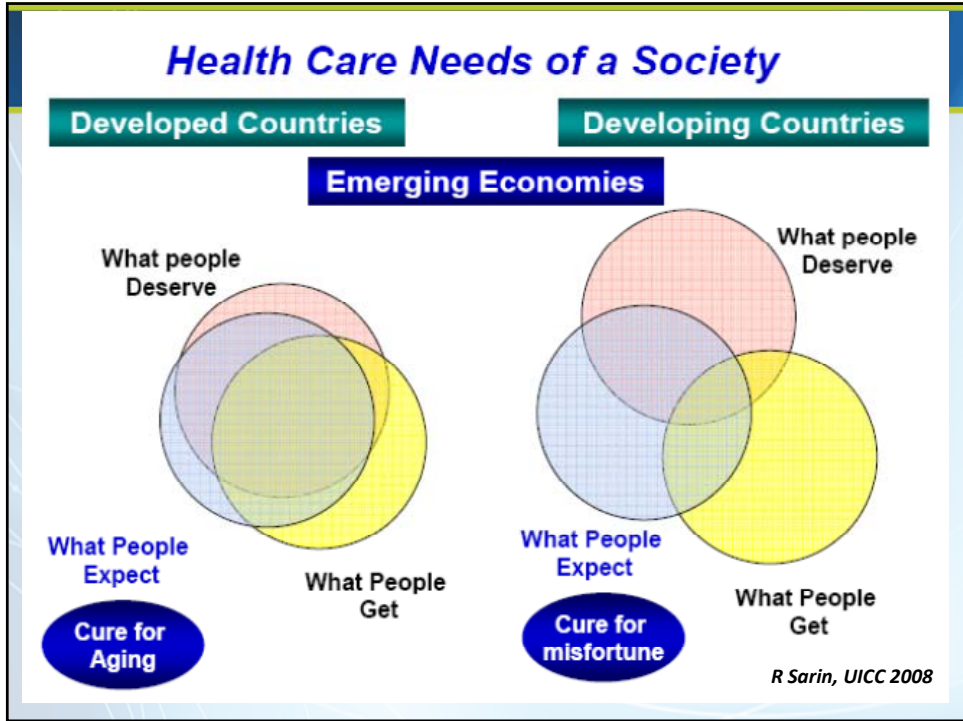
**Umesh Mahantshetty, DMRT, MD, DNB (RT)**

Department of Radiation Oncology  
Tata Memorial Hospital  
Mumbai, India

## **Disclosure**

Umesh Mahantshetty, DMRT, MD, DNB (RT), does not have any financial relationships or products or devices with any commercial interest related to the content of this activity of any amount during the past 12 months.

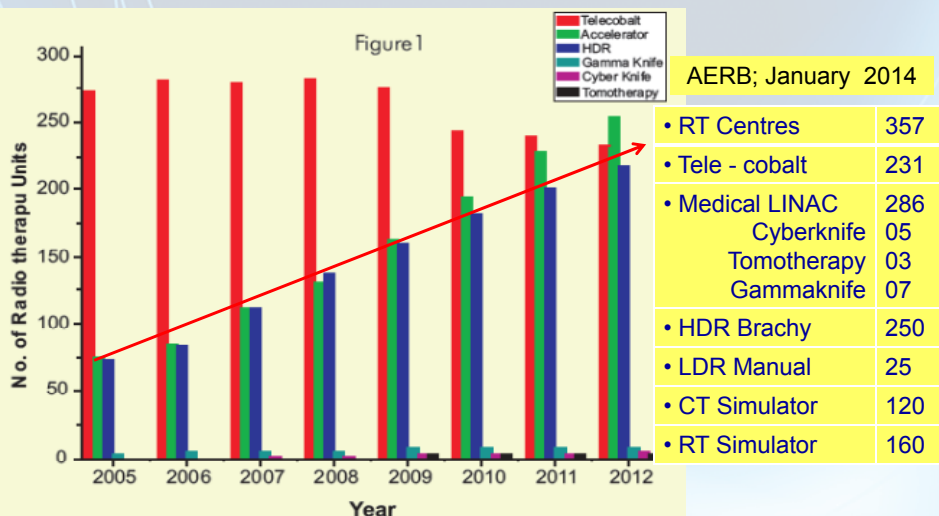






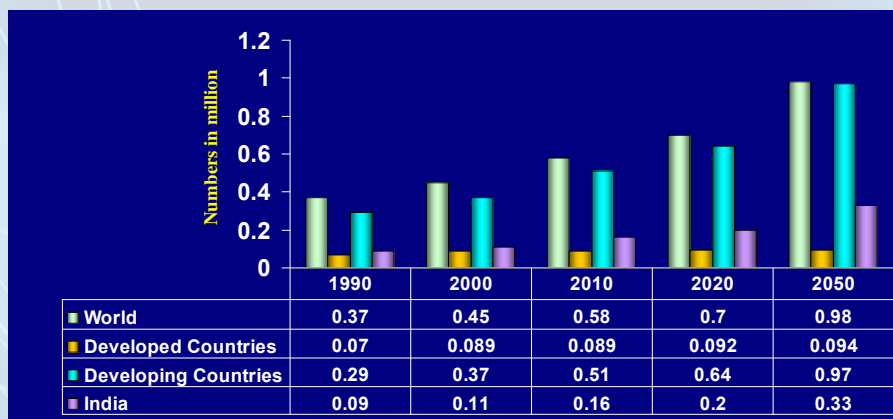


## Radiation therapy facilities in India



Atomic Energy Regulatory Board, India, Newsletter 2013

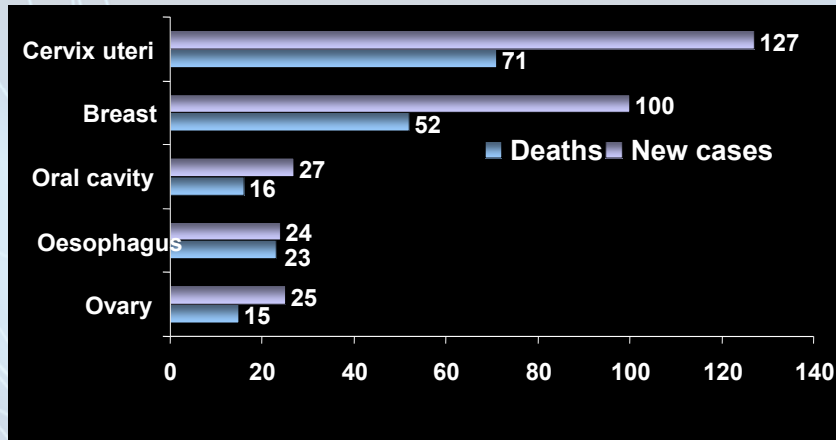
## Estimated number of new cases of Ca. Cervix 1990 - 2050



Source : Ferlay J, Parikh D.M. & Pisani P IARC, Lyon Globocan 2002



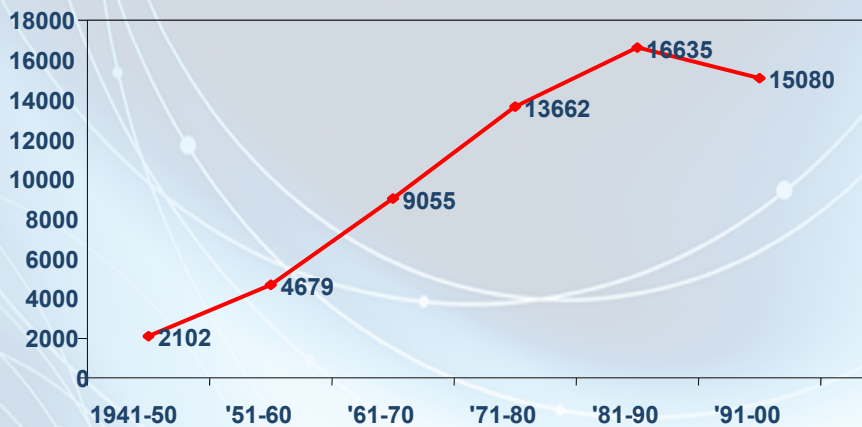
## Five Most Common Cancers in Indian Women Estimated No. of New Cases & Deaths (in Thousands): Year 2005\*



5 most common cancers account for almost two-thirds of total cases and deaths due to cancer in Indian women

\* estimated

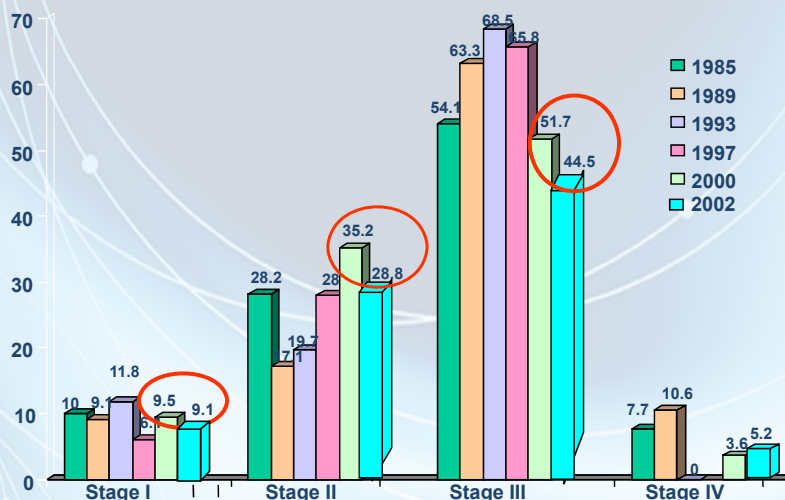
## Down the Decades Cancer Cervix: Tata Memorial Hospital 1941–2000





## Tata Memorial Hospital Cancer Registry 1985–2002

Down Staging of Carcinoma Cervix




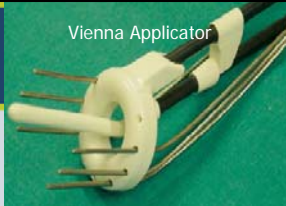
## Advances in Gynecological Brachytherapy Tata Memorial Hospital Experience

- Applicator development: *Intracavitary (IC), Interstitial (IS) & IC+IS*
- Incorporation of newer imaging modalities: *CT, MR, US, etc.*
- Advances in treatment planning systems
- **Image-/volume-based brachytherapy**



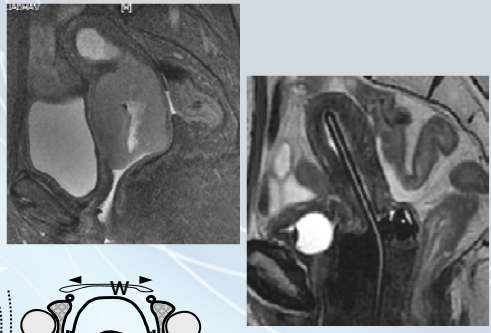
## In corporation of Newer Imaging Modalities

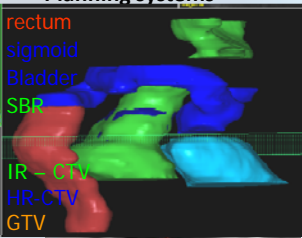
- 2D Planning : Orthogonal X-ray Based (STD)
- 3D Planning : TMH Experience
  - MRI: TMH-Initial Experience; *Int. J. Gynae Cancer: 2011*
  - US: TMH Experience; *Radio. Oncol 2012*
  - CT Scan: Interstitial Brachytherapy : *Brachytherapy 2013*
  - PET etc.
- Routine GYN Practice:
  - Average 6 (3- 9) Cx ICA/ daily + 1-2 Interstitial /wk cases
  - 3-4 X-ray; 2-3 CT; 1 MR Based Planning

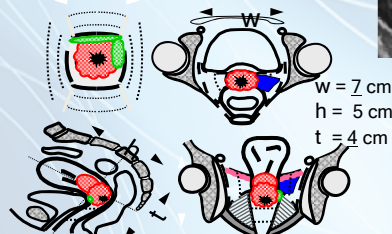



Vienna Applicator

- Applicators
- Imaging
- Planning systems



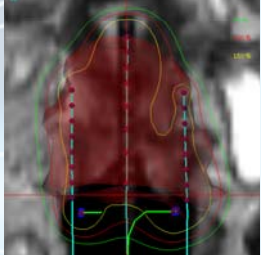




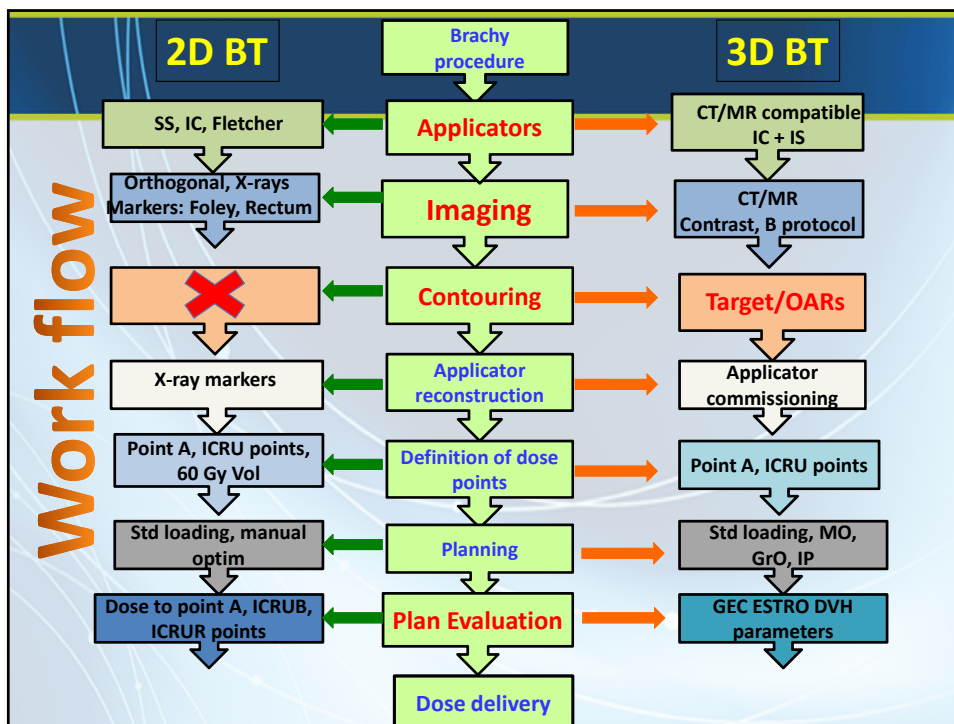
w = 7 cm  
h = 5 cm  
t = 4 cm

**"GOLD STANDARD"**

**Clinical drawing  
&  
MR Imaging**







## Brachytherapy Planning

- Brachytherapy : EUA, Appropriate Applicator placement
- MR Imaging : Bladder protocol, T2 axial, sagittal, coronal (3-5mm with 1 mm)  
(GEC-ESTRO RECOMMENDATION-IV)
- Contouring : Targets (GTV-B, HR-CTV, IR-CTV & OAR's (Rect, Blad, Sigm, SB)  
(GEC-ESTRO RECOMMENDATION-I)
- Planning : TPS (BrachyVision/Oncentra /Plato )
  - Catheter reconstruction (GEC-ESTRO RECOMMENDATION-III)
  - Loading pattern (Std with Needles ratio)
  - Optimization (Manual/Inverse)
- Plan evaluation : EQD2 values (GEC-ESTRO RECOMMENDATION-II)
  - Doses to HR-CTV, GTV (D90, D100, V100 etc...)
  - Doses to OAR's (rectum, bladder, sigmoid 0.1 cc, 1 cc, 2cc)





## MR Image-Based Brachytherapy TMH Experience

- 2006–2008: Retrospective & Feasibility Study
- 2009 onwards: International Collaboration with GEC-ESTRO and Participation in multi-centric studies (EMBRACE)
- 2013–2014: Future Studies

## Retrospective and Feasibility Study Dec 2006–May 2008 (N = 24)

International Journal of Gynecological Cancer:  
 August 2011 - Volume 21 - Issue 6 - pp 1110-1116  
 doi: 10.1097/IGC.0b013e31821caa55  
 Radiation Therapy

Reporting and Validation of Gynaecological Groupe Europeen de Curietherapie European Society for Therapeutic Radiology and Oncology (ESTRO) Brachytherapy Recommendations for MR Image-Based Dose Volume Parameters and Clinical Outcome With High Dose-Rate Brachytherapy in Cervical Cancers: A Single-Institution Initial Experience

Mahantshetty, Umesh MD, DNBR, DMRT\*; Swamidas, Jamema MSc, DRP\*; Khanna, Nehal MD\*; Engineer, Reena DNBR\*; Merchant, Nikhil H. MDT; Deshpande, Deepak D. DRP, PhD\*; Shrivastava, Shyamkishore MD, DNBR\*



	Vienna IC IJROBP2005	Vienna IC/IS IJROBP2005	Brabandere RO 2008	Lindegaard IJROBP2008	Chargari IJROBP 2008	TMH study IJGC 2011
<b>HRCTV</b>						
Vol in cc	34 +/- 17	44 +/- 27	48 +/- 19	34 +/- 12	36.3 ± 35	45.2 ± 15.8
D100	66 +/- 7	70 +/- 6	64 +/- 6	76 +/- 7	61.66 ± 7	53.9 ± 6.5
D90	87 +/- 10	96 +/- 12	79 +/- 7	91 +/- 10	74.85 ± 10	70.3 ± 10.6
Avg. PtA	89 +/- 8	93 +/- 9	79 +/- 5	92 +/- 9	71.4 ± 6	73.4 ± 4.5
<b>Bladder</b>						
Vol in cc	--	--	--	--	--	80.2 (20.3-235)
ICRU Bmax	75 +/- 16	73 +/- 19	74 +/- 15	67 +/- 31	63.7 ± 9	80.4 ± 34.4
D0.1cc	121 +/- 25	113 +/- 30	100 +/- 12	86 +/- 45	87.6 ± 12	136.0 ± 54.7
D2cc	83 +/- 9	83 +/- 14	82 +/- 6	73 +/- 16	71.7 ± 6	91.4 ± 24.6
<b>Rectum</b>						
Vol cc	--	--	--	--	--	33.4 (11-64.6)
ICRU Rmax	69 +/- 13	71 +/- 13	66 +/- 9	71 +/- 5	67.3 ± 8	63.5 ± 8.1
D0.1cc	77 +/- 10	77 +/- 9	64 +/- 5	71 +/- 10	70.6 ± 11	67.2 ± 9.9
D2cc	64 +/- 6	66 +/- 6	66 +/- 9	61 +/- 6	67.3 ± 8	57.9 ± 7.7
<b>Sigmoid</b>						
Vol cc	--	--	--	--	--	49.0 (14.5-97.5)
D0.1cc	79 +/- 12	84 +/- 14	82 +/- 13	79 +/- 13	72.7 ± 18	101.9 ± 45.2
D2cc	63 +/- 7	67 +/- 7	68 +/- 7	69 +/- 9	60.6 ± 6	74.4 ± 19.6

**Dosimetric Outcome** Mahantshetty et al, IJGC Aug. 2011

## Clinical Outcome

TMH Data (Dec 2006 – May 2008) (N = 24)

Median Follow-up: 18 (12–40) months

	Stage			Total N=24
	I B2 / IIA N=2	IIB N=10	IIIB N=12	
Local	--	2*	1#	3
Pelvic Node	--	--	1	1
Dist. metastasis	--	--	1	1
<b>Total</b>	--	<b>2</b>	<b>3</b>	<b>5</b>

\* Point A: 79 Gy and HR-CTV D90 doses: 56.5, 67 Gy;

# Point A: 70 Gy and HR-CTV D90 doses: 65 Gy;

Late sequelae: 1 pt with proctosigmoiditis

(0.1 and 2cc: R 46 & 64; S: 140 & 260 Gy)

Mahantshetty et al, Clin. Oncol. 2011 ; IJGC Aug. 2011



## TMH - AKH Collaboration: 2008-2009

R Potter and team  
AKH Vienna



## Tata Memorial Hospital Participation in International Multicentric Studies

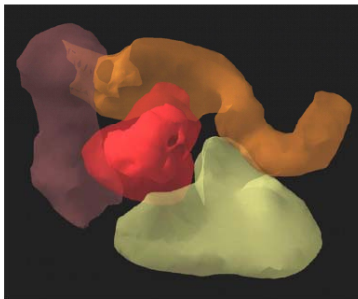
- Refine treatment standards

- International Recognition (GYN GEC-ESTRO Research Network)

A European study on MRI-guided brachytherapy  
in locally advanced cervical cancer

### EMBRACE

(ENDORSED BY GEC ESTRO)



A phase II Multicentric International Study by GEC - ESTRO Network



TMH EMBRACE Data	
Prospective MR-Based Brachytherapy <span style="float: right;">Dec. 2012</span>	
Total no. of patients	47/100 patients
Median age (range)	51 ± 8 (28-65) years
<b>Histology</b>	
Squamous carcinoma	40
Adenocarcinoma	05
Adenosquamous	02
<b>FIGO Stage (n)</b>	
IIB	18
IIIB	25
IVA	04
Intracavitary brachytherapy (HDR)	4 fractions of 7 Gy to HRCTV
Median follow-up (range)	16 ± 8.3 (7-36) months

DOSIMETRIC COMPARISON: Retrospective vs Prospective Data vs Literature					
	Vienna (IC)	VIE (IC/IS)	Brabandere	TMH: RD	TMH: PD
<b>HRCTV</b>					
Vol in cc	34 +/- 17	44 +/- 27	48 +/- 19	45.2 ± 15.8	42.5 ± 19.5
D100	66 +/- 7	70 +/- 6	64 +/- 6	54.1 ± 6.5	65.7 ± 4.6
D90	87 +/- 10	96 +/- 12	79 +/- 7	70.9 ± 10.6	87.2 ± 4.4
Avg. Pt A	82 +/- 9	--	79 +/- 5	73.4 ± 4.5	93.1 ± 24.8
<b>Bladder</b>					
ICRU Bladder	75 +/- 16	73 +/- 19	74 +/- 15	80.4 ± 34.4	76.4 ± 15.5
D0.1cc	121 +/- 25	113 +/- 30	100 +/- 12	139.1 ± 54.7	109.6 ± 19.7
D2cc	83 +/- 9	83 +/- 14	82 +/- 6	93.4 ± 24.6	74.8 ± 7.1
<b>Rectum</b>					
ICRU Rectum	69 +/- 13	71 +/- 13	66 +/- 9	63.5 ± 8.1	68 ± 7.9
D0.1cc	77 +/- 10	77 +/- 9	68 +/- 7	66 ± 9.9	71.5 ± 7.5
D2cc	64 +/- 6	66 +/- 6	62 +/- 4	57.8 ± 7.7	64. ± 5.5
<b>Sigmoid</b>					
D0.1cc	79 +/- 12	85 +/- 14	82 +/- 13	109.4 ± 45.2	74 ± 8.6
D2cc	63 +/- 7	67 +/- 7	68 +/- 7	74.6 ± 19.6	65.5 ± 5.4

Mahantsev et al. ESTRO 2013; Geneva





## TMH Data Clinical Outcomes (N = 47)

Median Follow-up : 16 ± 8.3 (7-36) months

	IIB N=18	IIIB N=25	IV N=04
Local alone	-	3	-
Pelvic node alone	1	-	-
Distant alone	1	2	-
LR + PR + DM	1	2	1
<b>Overall Local Recc</b>	<b>1 *</b>	<b>5*</b>	<b>1*</b>
<b>(HR-CTV D90 doses)</b>	<b>(88 Gy)</b>	<b>(76–86 Gy)</b>	<b>(87 Gy)</b>
<b>Total</b>	<b>3/18 (16.6%)</b>	<b>7/25 (28%)</b>	<b>1/4 (25%)</b>

\* Infield (HR-CTV) Recurrence

Mahantshetty et al, ESTRO 2013; Geneva

## Literature on Clinical Outcome: MR Image-Based Brachytherapy

CLINICAL OUTCOME	Vienna# N = 145 (IC + IS)	Paris ♦ N = 45	TMH 2006 § N = 24	TMH 2012 N = 47
FIGO Stage	I-IVA	IB-IVA	IB2-IIIB	IIB-IVA
ICA/IS	HDR	PDR	HDR	HDR
Median follow-up (range) in months	51	26 (9-47)	18 (12-40)	16 (6-36)
<b>Local control rates</b>	<b>87.5%</b>	<b>100*</b>	<b>91.5%</b>	<b>85%</b>
<b>Loco-regional control rates</b>	<b>86%</b>	<b>95%</b>	<b>87.5%</b>	<b>83%</b>
Rectal/sigmoid late sequelae (G3-4)	4%	5%	<1% so far	--
Bladder late sequelae (G3-4)	4%	6% (2%VVF)	--	---

\* 26/45 patients underwent hysterectomy

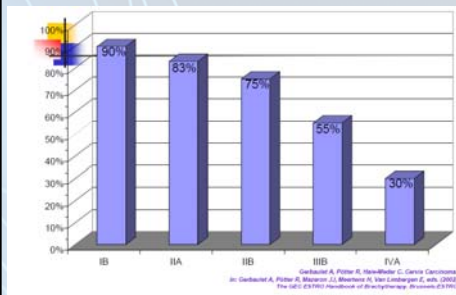
**EMBRACE Data : Final Analysis**

# RO 2007; ♦ IJROBP 2008; § IJGC 2011

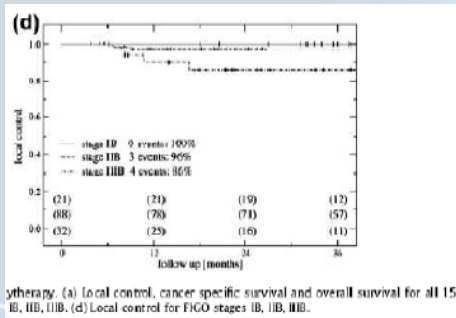


## Background

### 2D Brachy Robust data



### 3D Brachy Data emerging



Pötter et al. *Radiother Oncol* 2011

Local control rates:	2D	2D + CT	3D + CT	
IIB	75%	85%	96%	~ 11% ↑
IIIB	55%	65%	86%	~ 21% ↑

## LEVEL I EVIDENCE: 2013–2014

### Conventional X-ray Based 2D vs 3D MR Image-Based Brachytherapy in Cervical Cancers: A PHASE III RANDOMIZED CONTROL TRIAL (MULTICENTRIC)

Standard Arm: Conventional 2D X-ray based

Study Arm: 3D MR Image based

#### • Primary Endpoints:

1. Absolute benefit in local control rates by 10% for FIGO IIB and IIIB in study arm as shown in table below (defined a priori)
2. Non-inferiority for Grade 3/4 late toxicities: 480 pts in each arm

Alpha error: 0.05; Power: 80% 2 sided tailed test

FIGO Stage	Expected benefit	Sample size	Total
IIB	85–95% (10% benefit)	160 pts each arm	350*
IIIB	65–75% (10% benefit)	326 pts each arm	680*

\* Additional 30-50 pts for 10% lost to follow – up / violations

#### • Secondary Endpoints:

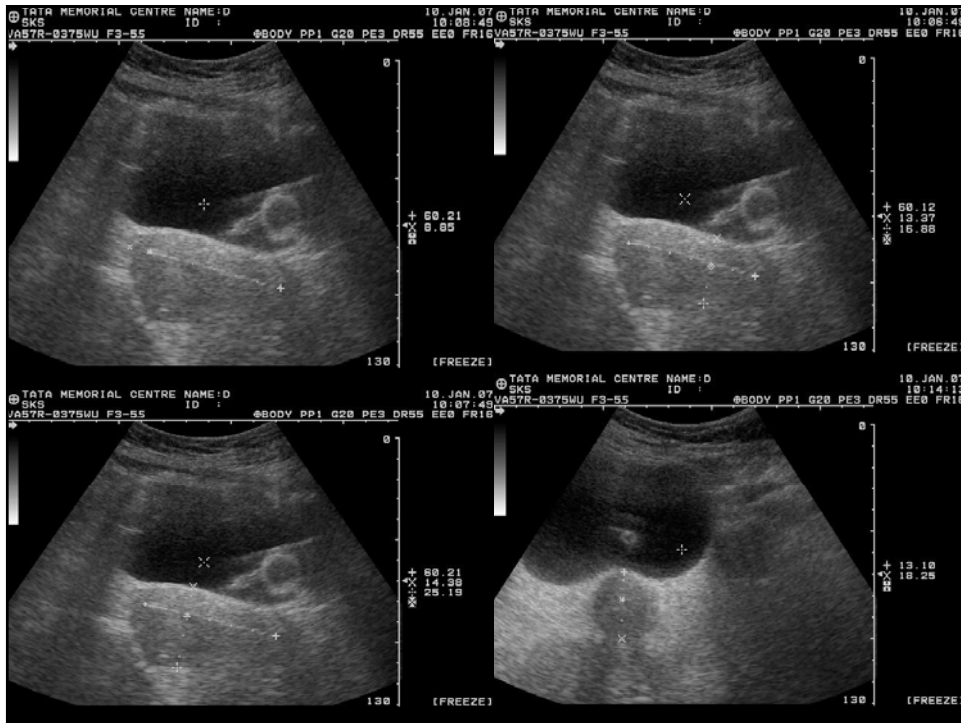
- Disease free and overall survivals

PI: TMH



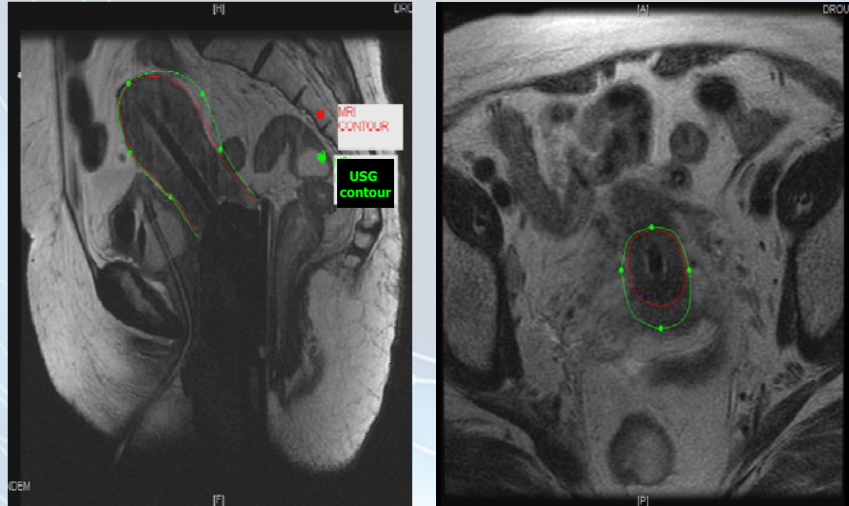
## US in Cx Brachytherapy

- Ultrasound-guided insertion of central tandem
  - Tandem length
  - Retroverted uterus
  - False passage
- Ultrasound-based planning
  - Uterine wall thickness
  - Bladder points
  - Rectal points
- Drawbacks
  - Coronal imaging not available
  - Posterior uterine surface not visible well





## Extrapolation of USG Contour Over MRI



Mahantshetty et al. Rad. Oncol. 2012

## USG and MRI Correlation (TMH Data)

- 32 Applications with MRI-Compatible Applicator
- Anterior Reference Points: **96%**
- Posterior Reference Points: **72%**
- Magnitude of Variation (>15%): **<8%**

*Significant Correlation between the USG and MRI Reference Points*

*Suggest: Use of USG for ICA Planning (21/2 D Planning)*

Mahantshetty et al. Rad. Oncol. 2012





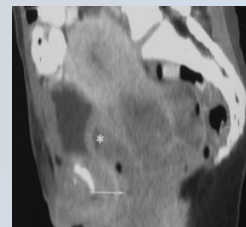
## SURVEY REPORTS

	2D	CT	MR	Others
United States (IJROBP 2010)	43%	55%	2%	US for insertion (55%)
Canada (Brachy 2013)	63%	66%	13%	9% (Cone beam CT)
Australia & NZ (JMIRO 2010)	30%	65%	-	20% (combination US+MR)
UK (Clin. Oncol. 2011)	29%	51%	20%	--
<b>GYN ESTRO TC Survey (AVG)</b>				
European Courses	45%	50%	30%	US (10%)
Outside Europe Courses	60%	40%	10%	US (15%)

*SURVEY in India: Ongoing (Indian Brachytherapy Society Initiative)*

## Why CT for “At Brachy Contouring”

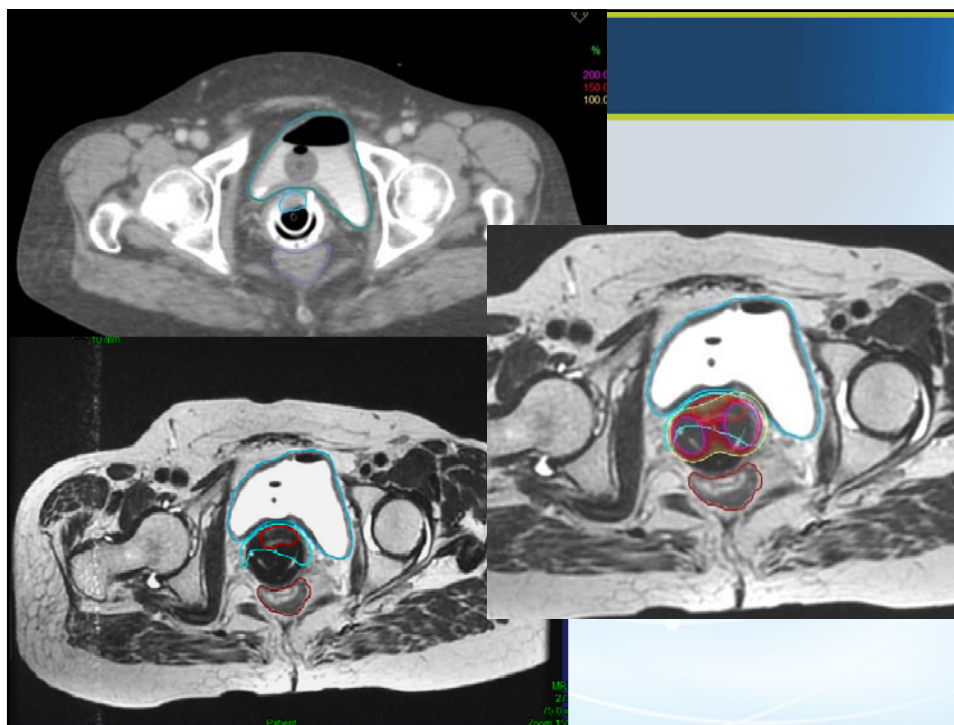
- Pros & Cons of CT Imaging
- Brachytherapy – Conventionally Point Based
- GEC-ESTRO Recommendations – 2005
  - Defined target and Organ at Risk
  - MRI – Imaging of choice
- Then Why CT?
  - CT Imaging: Gold STD for RT planning!
  - Vast experience with CT-based contouring!
  - Wide acceptability due to its use in XRT!
  - Availability: CT vs MR in RT department

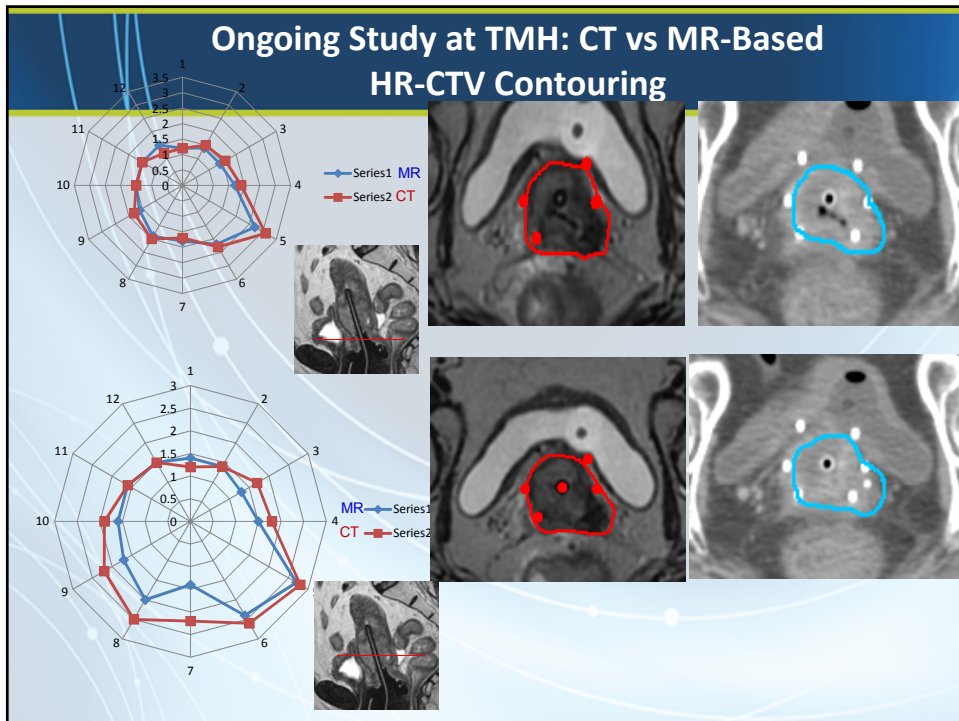
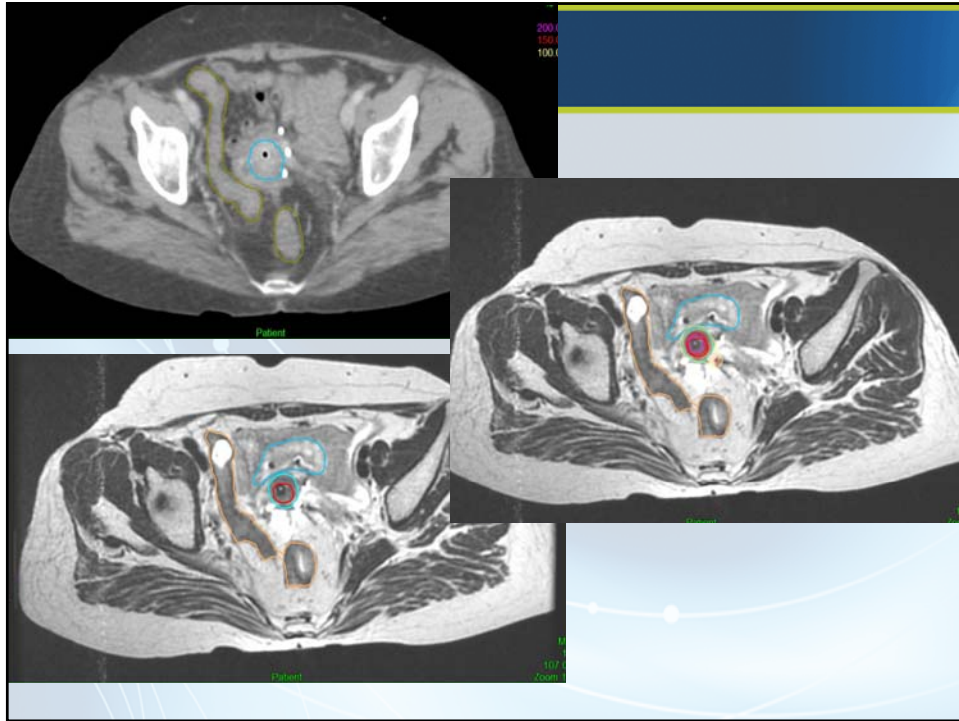




## Delineation of Target on CT

- **Experience of MR-Based Approach: Mandatory**
- **CT Imaging Protocol: IV Contrast, bladder filling...**
- **Target at brachytherapy**
  - GTV: poor visualization of residual tumor on CT
  - HRCTV: Clinical Drawing at Diagnosis and Brachy + CT imaging findings
  - IRCTV: margins to HR-CTV
- **HR-CTV: Practical & feasible contour possible on CT Imaging**
- **Defined conceptually as**
  - GTV-B + Whole of Cervix
  - With presumed extensions at brachy in:
    - Parametrium
    - Endocervical
    - Vagina









## SUMMARY AND CONCLUSIONS

- **Brachytherapy Set-ups: Steady Increase in facilities**
- **Image Based Brachytherapy: Implementation logistics still evolving**
- **Educational Programs: Workshops, Demo's more in developing world**
- **MR Image Based Brachytherapy Implementation in our setting: Challenge**
- **Alternate Imaging Modalities: Ongoing Research in our Settings**
- **Randomized trial: Poses a Bigger Challenge?**
- **Use of US: Potential in our settings, ongoing feasibility studies**



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- *GYN GEC-ESTRO Research Network*

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