IMAGE BASED / GUIDED BRACHYTHERAPY
IN
CERVICAL CANCERS

On behalf of Department of Radiation Oncology

Dr Umesh Mahantshetty, Associate Professor,
Tata Memorial Hospital,
Mumbai, India
IMAGE BASED / GUIDED BRACHYTHERAPY IN CERVICAL CANCERS

• Pre- Requisites

- Knowledge of cervical cancer biology & patterns of spread
- Basic knowledge of RT (XRT + ICBT) details
- Basics of ICBT procedure and planning

• Learning Objectives:

- Concepts of Image Guided / Based ICBT
- Various steps for Image Based Brachytherapy
- Proof of the Principle: Clinical Outcome & Evidence
• Technological advances in external radiation: Continues to be a success!

• Similar advances in Brachytherapy: but at Snails’ pace

• Brachytherapy: Oldest form of IMRT
BACKGROUND

Drawbacks of 2D Planning

• Limitations of Point A Based Dosimetry
• Target Volume Assessment
• Delineation of Organs at Risk
  - Rectum
  - Bladder
  - Sigmoid
  - Small intestine
  - Vaginal mucosa

• Brachytherapy: Conformal with Image Based
ADVANCES IN GYNAECOLOGICAL BRACHYTHERAPY

- Applicator development: *Intracavitary (IC), Interstitial (IS) & IC+IS*

- In corporation of Newer Imaging Modalities: *CT, MR, PET, etc.*

- Advances in Treatment Planning Systems

- *Image / Volume Based Brachytherapy*
Applicators Development

Vienna Applicator

CT Vienna System with Titanium Needles

CT MAC. Interstitial GYN Template
In corporation of Newer Imaging Modalities

- **2D Planning**: Orthogonal X-ray Based (STD)
- **3D Planning**:
  - US: TMH Experience (Reverse ICRETT)
  - CT Scan: Interstitial Brachytherapy
  - MRI: TMH Experience
  - PET etc.
ADVANCES IN GYN BRACHYTHERAPY PLANNING

CONVENTIONAL PLANNING

MRI BASED PLANNING

CT-BASED MUPIT PLANNING
CT Scan Based Planning

- Wide acceptability due to its use in external radiation therapy
- Bladder and Rectum visualization better
- Applicator Reconstruction: Easy
- Limitations:
  - Metal artifacts → special applicator
  - Poor differentiation b/w uterus, para-uterine tissue, cervix and tumor
INTERSTITIAL BRACHYTHERAPY IN CERVIX

INDICATIONS:
- Extensive Parametrial Disease
- Narrow/distorted vagina
- Post-hysterectomy Recc.
- Distal Vaginal involvement
- Persistent disease after radical RT

APPLICATORS:
- Syed-Neblett Template (LDR)
- Martinez Universal Perineal Interstitial Template (MUPIT-HDR)

*Complication rates requiring surgical intervention are high*

*IJROBP 1985, GYNAE ONCOL 1995;*
Technique

Spinal Anesthesia

Silver markers

Template placement

Needle placement: Anterior and lateral

Under per-rectal guidance / TRUS / MR based
Perineal Interstitial HDR Brachytherapy

Martinez Universal Perineal Interstitial Template

- EUA: Residual disease, pelvic anatomy etc. assessed
- 18 G stainless needles, multiple plane implant
- CT Scan images with 3-5 mm slice thickness
- Image acquisition and Delineation
- Treatment planning:
  - Catheter reconstruction and Source loading (6-6.5 cm)
  - Basal dose points (Paris Dosimetry system)
  - Dose prescription: 3.4 – 4 Gy per fraction @ 2# per day 6 hrs apart x 4-5#
  - Optimization: Geometric +/- graphical
  - Plan evaluation (DVH): Target and OAR’s
Implant Orientation and Needle identification is very important

- Dosimetry
- Dose: 3.4 – 4 Gy /fraction
- 2 fractions per day 6 hours apart
- No of fractions: 4-6 depending on the response
MUPIT - HDR : TMH Experience

MEAN FU : 30 MONTHS (MEDIAN 28 mths)

<table>
<thead>
<tr>
<th></th>
<th>Post Inadvertant Sx CA cervix (N=45)</th>
<th>CA VAULT (N=68)</th>
<th>CA VAGINA (N=22)</th>
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<tbody>
<tr>
<td><strong>CONTROLLED</strong></td>
<td>27 (60%)</td>
<td>42 (61.8%)</td>
<td>14 (63.6%)</td>
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<tr>
<td><strong>PERSISTANT DIS</strong></td>
<td>4 (8.9%)</td>
<td>5 (7.4%)</td>
<td>1 (4.5%)</td>
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<tr>
<td><strong>CENTRAL RECC</strong></td>
<td>9 (20%)</td>
<td>16 (23.5%)</td>
<td>3 (13.6%)</td>
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<tr>
<td><strong>LOCO-REGIONAL</strong></td>
<td>2 (4.4%)</td>
<td>1 (1.5%)</td>
<td>2 (9.1%)</td>
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<tr>
<td><strong>L-R + DISTANT</strong></td>
<td>1 (2.2%)</td>
<td>3 (4.4%)</td>
<td>2 (9.1%)</td>
</tr>
<tr>
<td><strong>DISTANT</strong></td>
<td>2 (4.4%)</td>
<td>1 (1.5%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
Late toxicity

• 4 pts: Grade III RT Proctitis

• 2 pts Grade IV rectal (RVF: had disease)

• Poor documentation of late sequlae
MRI Based Brachytherapy Planning

- Good soft tissue contrast
- True multi-planar imaging
- Differentiation between cervix, uterus, tumor and para-uterine tissue
- Rectum, bladder, sigmoid and small intestine visualized
- Limitations:
  - Expensive
  - Special applicator
  - Logistics

MR Based ICA in use last 6 - 9 years now
Understanding of MR Pelvic anatomy: Vital
GEC - ESTRO RECOMMENDATIONS
Dose Volume Parameters for Targets & OAR’s

D100, D90 for GTV, HR CTV, IR CTV

D0.1cc, D1cc, D2cc for OARs

Radiother and Oncol 2006; IJROBP 2007
Example: Stage IB2
GEC-ESTRO recommendations

Tumor at time of diagnosis.
MR IBB in Cx Cancers: TMH Protocol

- **GYN Joint Clinic Staging**
- Planned for Radical RT +/- CT (weekly Cisplatin 40 mg/m2 x 4-5#)
- External + MR Based Brachytherapy (4th – 5th week onwards)
- Applicators: MR Compatible Tandem Ovoids / Ring / Interstitial
- MR Protocol:
  - 1.5 T with body coil
  - FSE T1 as localizer + FSE T2 (axial, saggital and coronal)
    with 3 - 4 mm slice thickness and 0 - 1 mm slice gap
- Target Volumes: GTV, HR - CTV, IR - CTV
- OAR’s: Rectum, Bladder and Sigmoid (0.1, 1, 2 cc)
- Doses: EQD2 values
• **GTV:** macroscopic tumour extension at time of brachytherapy…

**High signal intensity mass(es)** (FSE, T2) in cervix/corpus, parametria, vagina, bladder and rectum

• **HR-CTV:** includes **gtv, whole cervix, and presumed extracervical tumour extension.** Pathologic residual tissue(s) as defined by palpable indurations and/or grey zones in parametria, uterine corpus, vagina or rectum and bladder are included in HR-CTV. No safety margin are added.

• **IR-CTV:** encompasses the **HR-CTV different safety margins** are added according to the treatment strategy, tumour size and tumour regression. **In any case a minimal safety margin of 5 to 15 mm** have to be added.
Clinical Drawing

At Diagnosis

w = 7 cm
h = 5 cm
t = 4 cm
• XRT: Pelvis
• 3DCRT / IMRT
• Dose: 45 – 50 Gy
• Concomitant weekly Cisplatin (40 mg / m²)
• Assess for Brachytherapy boost
Brachytherapy Planning

- **Brachytherapy**: EUA, Appropriate Applicator placement
- **MR Imaging**: Bladder protocol, T1 / T2 axial, sagittal, coronal (3mm with 1mm)
- **Contouring**: Targets and OAR’s
- **Planning**: TPS (Brachyvision / Oncentra / Plato)
  - Catheter reconstruction
  - Loading pattern (Std with Needles ratio)
  - Optimization (Manual / Inverse)
- **Plan evaluation**: EQD2 values
  - Doses to HR-CTV, GTV (D90, D100, V100 etc…)
  - Doses to OAR’s (rectum, bladder, sigmoid 0.1 cc, 1 cc, 2cc)
CONTOURING

rectum
sigmoid
Bladder
SBR
IR-CTV
HR-CTV
GTV
CATHETER RECONSTRUCTION

- Direct reconstruction from MR Images
- Variation < 2 mm

APPROPRIATE LOADING

- Std ICA loading
- Load Interstitial needles
PLAN EVALUATION
PLAN EVALUATION

ICA Vs ICA + IS

- Higher HR-CTV / IR-CTV doses
- Without significant increase in doses to OAR's
Key points

- Imaging and Contouring of Target & OAR’s Protocol
- Treatment planning
  - Catheter reconstruction
  - HR-CTV Volume based Optimization (Point A based)
  - Loading patterns & optimum ratio of Std Vs Interstitial
  - Standard loading followed by manual optimization: Safe
  - Documentation of DVH Parameters
- Individualized plan for each application: to minimize inter-fraction variation
- Treatment Delivery: QA check
- Team work: Radiologist, Rad Oncologist, Med Physicist, Dosimetrist & Tech
- Small learning Curve
Results – Optimization and CTV / GTV
(Vienna 1998-2003)

Mean Values for **Point A left and right:** $79 \pm 10$ Gy\(_{\alpha\beta10}\)

<table>
<thead>
<tr>
<th></th>
<th><strong>High Risk CTV</strong></th>
<th><strong>GTV</strong></th>
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<tbody>
<tr>
<td>Volume</td>
<td>36</td>
<td>12 cm(^3)</td>
</tr>
<tr>
<td>D100 (minimum target dose)</td>
<td>65</td>
<td>90 Gy(_{\alpha\beta10})</td>
</tr>
<tr>
<td>D90</td>
<td>86</td>
<td>123 Gy(_{\alpha\beta10})</td>
</tr>
<tr>
<td>V100</td>
<td>87</td>
<td>97 %</td>
</tr>
</tbody>
</table>

*Based on 145 patients with individual MRI based treatment plans*

*Dimopoulos et al. 2009, Pötter et al. 2007*
3D-based Dose Volume Parameters for OAR

CLASSICAL MAX DOSE: in 3D
no clinical relevant endpoint

FIXED VOLUME: tolerance dose (total dose) -
“minimum dose to the most exposed tissue”*

1 cc/2 cc: teleangiectasia
(20 mm x 20 mm x 5 mm)

0.1 cc: 3D “maximum dose“:
ulceration (fistula)

* GYN GEC ESTRO Recommendations(II)
Radiother Oncol 2006
N = 35 patients with Dose volume effects for rectal morbidity applying GEC ESTRO recommendations

Koom et al. IJROBP 2007

P. Georg et al. Radioth&Oncol 2009

![Graph showing incidence of VRS ≥ 3 and LENT/SOMA ≥ 2 as a function of dose.](image)

![Graph showing probability of score ≥ 2 as a function of EQD±.](image)

![Graph showing incidence of late side effects ≥ 2 as a function of D2cc.](image)

![Graph showing relationship between D2cc and late side effects in the rectum.](image)

Koom et al. IJROBP 2007

P. Georg et al. IJROBP 2011
## Results – DVH values / ICRU reference points

### Bladder

<table>
<thead>
<tr>
<th></th>
<th>D&lt;sub&gt;2cc&lt;/sub&gt;</th>
<th>D&lt;sub&gt;0.1cc&lt;/sub&gt;</th>
<th>ICRU point dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>95 (±22) Gy&lt;sub&gt;αβ3&lt;/sub&gt;</td>
<td>162 (±75) Gy&lt;sub&gt;αβ3&lt;/sub&gt;</td>
<td>72 (±15) Gy&lt;sub&gt;αβ3&lt;/sub&gt;</td>
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</tbody>
</table>

### Rectum

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<thead>
<tr>
<th></th>
<th>D&lt;sub&gt;2cc&lt;/sub&gt;</th>
<th>D&lt;sub&gt;0.1cc&lt;/sub&gt;</th>
<th>ICRU point</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>65 (±12) Gy&lt;sub&gt;αβ3&lt;/sub&gt;</td>
<td>86 (±27) Gy&lt;sub&gt;αβ3&lt;/sub&gt;</td>
<td>67 (±13) Gy&lt;sub&gt;αβ3&lt;/sub&gt;</td>
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</tbody>
</table>

### Sigmoid

<table>
<thead>
<tr>
<th></th>
<th>D&lt;sub&gt;2cc&lt;/sub&gt;</th>
<th>D&lt;sub&gt;0.1cc&lt;/sub&gt;</th>
</tr>
</thead>
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<tr>
<td></td>
<td>62 (±12) Gy&lt;sub&gt;αβ3&lt;/sub&gt;</td>
<td>78 (±12) Gy&lt;sub&gt;αβ3&lt;/sub&gt;</td>
</tr>
</tbody>
</table>

Biologically weighted to 2 Gy/fraction, α/β=3 Gy

Based on 145 patients with individual MRI based treatment plans (Vienna) (Georg et al. 2011 IJROBP)
### Total no of patients
- **24**

### Median Age (range)
- **45 (35-65) years**

### Histology
- **Squamous Carcinoma**

### FIGO Stage (n)
- **IB2/IIA**: 2
- **IIB**: 10
- **IIIB**: 12

### Intracavitary Brachytherapy (HDR)
- 3-5 fractions of 7 Gy to point A once weekly

### Median follow-Up (Range)
- **18 (12 – 40) months**

*Mahantshetty et al, IJGC  Aug. 2011*
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</tr>
<tr>
<td>Vol in cc</td>
<td>34 +/- 17</td>
<td>44 +/- 27</td>
<td>48 +/- 19</td>
<td>34 +/- 12</td>
<td>36.3 ± 35</td>
<td>45.2 ± 15.8</td>
</tr>
<tr>
<td>D100</td>
<td>66 +/- 7</td>
<td>70 +/- 6</td>
<td>64 +/- 6</td>
<td>76 +/- 7</td>
<td>61.66 ± 7</td>
<td>53.9 ± 6.5</td>
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<tr>
<td>D90</td>
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<td>79 +/- 7</td>
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<td>74.85 ± 10</td>
<td>70.3 ± 10.6</td>
</tr>
<tr>
<td>Avg. Pt A</td>
<td>89 +/- 8</td>
<td>93 +/- 9</td>
<td>79 +/- 5</td>
<td>92 +/- 9</td>
<td>71.4 ± 6</td>
<td>73.4 ± 4.5</td>
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<td>Vol in cc</td>
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<td>--</td>
<td></td>
<td>80.3 (20.3-235)</td>
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<tr>
<td>ICRU Bmax</td>
<td>75 +/- 16</td>
<td>73 +/- 19</td>
<td>74 +/- 15</td>
<td>67 +/- 31</td>
<td>63.79 ± 9</td>
<td>80.4 ± 34.4</td>
</tr>
<tr>
<td>D0.1cc</td>
<td>121 +/- 25</td>
<td>113 +/- 30</td>
<td>100 +/- 12</td>
<td>86 +/- 45</td>
<td>87.6 ± 12</td>
<td>136.0 ± 54.7</td>
</tr>
<tr>
<td>D2cc</td>
<td>83 +/- 9</td>
<td>83 +/- 14</td>
<td>82 +/- 6</td>
<td>73 +/- 16</td>
<td>71.7 ± 6</td>
<td>91.4 ± 24.6</td>
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<td><strong>Rectum</strong></td>
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<tr>
<td>Vol cc</td>
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<td>101.9 ± 45.2</td>
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**Dosimetric Outcome**

*Mahantshetty et al, IJGC Aug. 2011*
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- HR CTV volumes higher
- Sigmoid and Bladder Doses higher
## EVIDENCE

**TMH Data (Dec 2006 - May 2008) (N = 24)**

**Median Follow-up : 18 (12 - 40) months**

### Treatment Outcome

<table>
<thead>
<tr>
<th>Stage</th>
<th>IB2 / IIA N=2</th>
<th>IIB N=10</th>
<th>IIIB N=12</th>
<th>Total N=24</th>
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<tr>
<td>Local</td>
<td>--</td>
<td>2*</td>
<td>1#</td>
<td>3</td>
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<tr>
<td>Pelvic Node</td>
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<td>1</td>
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<tr>
<td>Dist. metastasis</td>
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<td>1</td>
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<tr>
<td>Total</td>
<td>--</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
</tbody>
</table>

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

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

Late sequelae: 1 pt with proto-sigmoiditis

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

<table>
<thead>
<tr>
<th>CLINICAL OUTCOME</th>
<th>Vienna# N = 145</th>
<th>Paris ♦ N = 45</th>
<th>TMH$ N = 24</th>
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<tbody>
<tr>
<td>FIGO Stage</td>
<td>I-IVA</td>
<td>IB-IVA</td>
<td>IB2-IIIB</td>
</tr>
<tr>
<td>ICA/IS</td>
<td>HDR</td>
<td>PDR</td>
<td>HDR</td>
</tr>
<tr>
<td>Median Follow-up (Range) in mths</td>
<td>51</td>
<td>26 (9-47)</td>
<td>12 (6-36)</td>
</tr>
<tr>
<td>Local Control Rates</td>
<td>87.5%</td>
<td>100*</td>
<td>91.5%</td>
</tr>
<tr>
<td>Loco-regional Control Rates</td>
<td>86%</td>
<td>95%</td>
<td>87.5%</td>
</tr>
<tr>
<td>Rectal/Sigmoid late sequelae (G3-4)</td>
<td>4%</td>
<td>7%</td>
<td>&lt;1% so far</td>
</tr>
<tr>
<td>Bladder late sequelae (G3-4)</td>
<td>4%</td>
<td>8% (VVF)</td>
<td>--</td>
</tr>
</tbody>
</table>

* 26/45 patients underwent hysterectomy  

# RO 2007; ♦ IJROBP 2008; $ IJGC Aug. 2011
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

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 (2D Planning)

Conformal brachytherapy planning for cervical cancer using transabdominal ultrasound.

Van Dyk S, Narayan K, Fisher R, Bernshaw D.
Radiation Therapy Services, Peter MacCallum Cancer Centre, East Melbourne, Victoria, Australia. sylvia.vandyk@petermac.org

Abstract

PURPOSE: To determine if transabdominal ultrasound (US) can be used for conformal brachytherapy in cervical cancer patients.

MATERIALS AND METHODS: Seventy-one patients with locoregionally advanced cervical cancer treated with chemoradiation and brachytherapy were included in this study. The protocol consisted of US-assisted tandem insertion and conformal US-based planning. Orthogonal films for applicator reconstruction were also taken. A standard plan was modified to suit the US-based volume and treatment was delivered. The patient then underwent a magnetic resonance imaging (MRI) scan with the applicators in situ. Retrospectively, individual standard (STD), US, and MRI plans were extrapolated for five fractions and superimposed onto the two-dimensional sagittal MRI images for comparison. Doses to Point A, target volume, International Commission on Radiation Units and Measurements (ICRU) 38 bladder and rectal points, and individualized bowel points were calculated on original implant geometry on Plato for each planning method.

RESULTS: STD (high-dose-rate) plans reported higher doses to Point A, target volume, ICRU 38 bladder and rectal points, and individualized bowel point compared with US and MRI plans. There was a statistically significant difference between standard plans and image-based plans—STD vs. US, STD vs. MRI, and STD vs. Final—having consistent (p < or = 0.001) respectively for target volume, Point A, ICRU 38 bladder, and bowel point. US plan assessed on two-dimensional MRI image was comparable for target volume (p = 0.11), rectal point (p = 0.8), and vaginal mucosa (p = 0.13). Local control was 90%. Late bowel morbidity (G3, G4) was 2%.

CONCLUSIONS: Transabdominal ultrasound offers an accurate, quick, accessible, and cost-effective method of conformal brachytherapy planning.

Conclusions: Transabdominal US offers accurate, quick and cost-effective method of conformal brachytherapy planning.
SUMMARY AND CONCLUSION

- Brachytherapy should be integral part of Radical radiation therapy

- Conventional planning, though time tested, merits refinement
  - Incorporation of better Imaging
  - Optimization in planning including contouring
  - Documentation and uniform reporting

- Generate robust data with the above: CT Vs MR Based brachytherapy

- MR Image Guided Brachytherapy: Initial experience enterprising

- Outcome study: EMBRACE Study

- Use of US: Potential in our settings, needs further evaluation

- Strengthen Brachytherapy skills: “Improved Therapeutic Window”
Future Directions

- Further refinement of Applicators
- Advances in Treatment Planning: Cumulative Doses,
- Radiobiological modeling for tumor and OAR’s
- Multifunctional MRI, Perfusion - diffusion regions and dose escalation
Acknowledgements:

- Departments of Radiation Oncology & Medical Physics
- GYN Disease Management Group TMC
- Patients

Tata Memorial Hospital Complex, Mumbai, India