IMAGE BASED
BRACHYTHERAPY FOR
CERVICAL CANCER

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Image Based Brachytherapy

- Image *guided* brachytherapy
  - Technique where imaging is used to guide brachytherapy applicator/source placement.

- Image *based* brachytherapy
  - Technique where advanced imaging modalities are used to gain information regarding the volumetric dose distribution.
Historically

Dose prescription & treatment planning have been mainly based on traditional schools using a certain system, including a given technique, loading pattern, & dose rate.

“Manchester”, “Stockholm”, “Fletcher/MD Anderson”

Current practice is to prescribe dose to **Point A**

Empiric point, does not reflect dose to tumor, reference is with applicator, is located where **dose gradient is high** i.e. about **10%/mm**.
Historically


- Dose be specified in terms of total reference air kerma TRAK
- Reference volume be determined – tissue volume encompassed by a reference isodose surface, 60 Gy
- Points for dose assessment to bladder & rectum
- Extended to dose-volume histograms DVH for OARs.
- Compare brachytherapy performed in different institutions.

- Applied only minimally, no correlation with primary cervical tumor control.
Recently

3D & 4D image–based brachytherapy treatment planning & dosimetry has been used for Cancer Cervix.

Prescribed dose is always related to the target while the actual coverage can be evaluated with the use of DVH parameters.

Shape the spatial dose to conform to the target volume

- Reduce dose to normal tissues & hence reduce the normal tissue toxicity.
- Escalate dose to the tumor to produce greater rates of local control.
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- Imaging modalities used
  - Ultrasonography
  - Fluoroscopy
  - Computed tomography CT
    - 3D anatomic relationship of applicator & neighbouring structures
    - Difficult to separate cervical tumor from uterus, rectum & bladder & to ascertain where cervix ends & vagina begins

- MRI  T2-weighted images: High signal intensity,
  After ERT: intermediate signal intensity (grey zones)

- PET
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- Imaging modalities used
  - MRI Scan
    - Superior soft tissue resolution & is **the best imaging modality for visualisation of cervical tumor size, volume & extent**
    - Distinction of tumor from normal uterus & cervix
    - Definition of parametrial, & vaginal infiltration of disease
    - Visualise the anatomic relationship between applicator & tumor & adequacy of radiation coverage
    - Doses to rectum & bladder can be assessed
    - **Multiplanar scanning capabilities**-coronal, sagittal & axial
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CT SCAN

MRI SCAN
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- Imaging modalities used

  - **MRI Scan** – disadvantages
    - **MRI – compatible applicator** made of nonferromagnetic materials. Titanium & zirconium alloy needles.
    - **Bony anatomy** not differentiated as well as on CT

  - **Treatment planning systems use Hounsfield numbers** hence they are not able to use MRI scans directly & it is necessary to fuse MRI with CT scans
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- Imaging modalities used

- **MRI Scan accuracy**
  - Tumor volume - 93%
  - Deep stromal invasion - 94%
  - Parametrial infiltration - 87-94%
  - Lymph node involvement - 72-93% similar to CT
  - Overall Staging - 76-89% better than CT, USG, Clinical
Requirements

- Imaging
- ‘Image-able’ & artifact free applicator
- Applicator fixation & immobilization
- Treatment planning system
- Compatible communication protocol-DICOM, so that the treatment planning system can interpret the images
- CT & MRI data sets need to be registered to superimpose one set on another
- Contouring tumor & OARs
- Dosimetry & dose-volume parameters for tumor & OARs
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- Tumor volume assessment
  - First based on **Clinical Examination**
  - Appropriate **documentation** in three dimensions
  - **Sectional imaging** gives information on tumor extension & configuration & its topography
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TUMOUR EXTENSION AND PARAMETERS AT DIAGNOSIS

axial  sagittal  coronal
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### Tumour Response: Good

<table>
<thead>
<tr>
<th>Diagnosis: involvement of the right proximal parametrium</th>
<th>Volume</th>
<th>Width</th>
<th>Thickness</th>
<th>Height</th>
<th>Distance PSW right</th>
<th>Distance PSW left</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>88 cm³</td>
<td>5 cm</td>
<td>5 cm</td>
<td>7 cm</td>
<td>4 cm</td>
<td>5 cm</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Brachytherapy: minimal residual extension into the right parametrium</th>
<th>Volume</th>
<th>Width</th>
<th>Thickness</th>
<th>Height</th>
<th>Distance PSW right</th>
<th>Distance PSW left</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9 cm³</td>
<td>3 cm</td>
<td>2 cm</td>
<td>3 cm</td>
<td>5 cm</td>
<td>6 cm</td>
</tr>
</tbody>
</table>
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- **Target Volume**
  - **GTV**
    - Includes macroscopic tumor extension as detected by clinical examination (visualisation & palpation) & as visualised on MRI
  - Change of GTVs during treatment –
    - At diagnosis $\text{GTV}_D$
    - At brachytherapy $\text{GTV}_B$
The GTV encompasses the macroscopic tumour extension at time of brachytherapy: high signal intensity mass(es) (FSE, T2) in cervix/corpus, parametria, vagina, bladder and rectum.
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Target definition

2 CTVs

A first target related to the extent of GTV at time of BT:
- taking into account tumour extent at diagnosis.

- **High risk CTV**
  - Major risk of recurrence because of residual macroscopic tumor
  - Intent is to deliver a total dose as high as possible to eradicate all residual macroscopic tumor
  - *High dose prescribed to this target (80-90+Gy)=dose to point A*
Target definition

2 CTVs

A second target related to the extent of GTV at diagnosis:

- **Intermediate risk CTV**

  - Major risk of recurrence in areas that initially had macroscopic extent of disease with residual *microscopic* disease at time of BT
  - Intent is to deliver dose appropriate to cure *microscopic disease in cervix cancer*, which corresponds to a dose of 60Gy
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Three different target volumes according to cancer cell density

Pelvic wall region
Potential microscopic tumour spread

Macrosopic tumour load

Potential microscopic tumour spread

Significant microscopic disease

Significant microscopic disease

HR: High risk CTV
IR: Intermediate risk CTV
LR: Low risk CTV
Haie-Meder, Radiot & Oncol, 74, 2005
The HR-CTV includes GTV, whole cervix, and presumed extracervical tumor 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.
HR-CTV encompasses IR-CTV with a safety margin of 5-15 mm. Amount of safety margin is chosen according to tumour size an location, potential tumour spread, tumour regression and treatment strategy.
OARs

- Contouring organ wall volumes is difficult
- For organ wall volumes **upto 2-3 cm³**, organ & organ wall contouring lead to almost identical numerical results this allows for organ contouring only
- If larger organ wall volumes are considered organ wall contouring has to be performed

- When assessing the late effects from **brachytherapy**, small organ (wall) volumes irradiated to a high dose seems to be of major interest.
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Dose prescription

- The prescribed dose is always related to the target.

- The prescription dose is the planned dose to cover this target as completely as possible.

- Coverage of the target can be improved starting from the standard dose prescription & careful adaptation of the loading pattern & dwell times.
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Cervix Carcinoma
Alain Gerbaulet, Richard Pötter, Christine Haie-Meder
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- **Dose prescription**
  - **HR-CTV Dose**
    - Small tumor - 80-85 Gy
    - Large tumor, good response - 85-90 Gy
    - Large tumor, poor response - 90+ Gy
  - **IR-CTV ~ 60 Gy**

- **V(60 Gy_{EQD2})** plays a role for evaluating the IR CTV
- **V(85 Gy_{EQD2})** represents more closely the prescription dose to the HR CTV

- For comparison, dose reporting should refer to the prescribed dose to the image-based target & to the traditional system - point A
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- Parameters for dosimetric evaluation
  GTV/CTV

- ** Prescribed Dose - PD **
- ** D100 & D90 ** – minimum dose delivered to 100 & 90% of the volume of interest respectively
- D100 is extremely dependent on target delineation. Due to steep dose gradients, small spikes in the contour cause large deviations in D100
- ** D90 ** is less sensitive to these influences & is therefore considered a more ‘stable’ parameter

- ** TRAK **
- ** Point A Dose **
- ** V 100 ** – Volume receiving ≥ 100%of PD
- ** V150/200 ** – Volume receiving 150%/200%of PD
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- **Dose volume parameters**
  - Coverage of target volumes can be derived from **cumulative DVH** analysis
  - DVHs for GTV & CTV in I/C brachytherapy have a plateau-100% dose coverage of the volume of interest
  - Plateau goes down smoothly indicating decreasing % of dose coverage with increasing dose

*Potter, Radiat & Oncol, 78, 2006*
OARs

As there is a rapid dose fall-off near the sources, in particular in adjacent small organ (wall) volumes, dose assessment has to refer to one (or more) defined dose points in these limited volumes.

The minimum dose in the most irradiated tissue volume adjacent to the applicator (0.1, 1, 2, 5 cm³) is recommended for recording & reporting.

It is assumed that these volumes are contiguous.

This is wrongly called as the ‘maximum dose’ to a 2 cm³ tissue.
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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)

2 cm³

0.1 cm³

*GYN GEC ESTRO Recommendations (II)
Radiotherapy and Oncology 2006
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Potter, Radiol & Oncol, 78, 2006
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- Dose volume constraints
  - 2 cm³ of rectum & sigmoid: $< 75 \text{ Gy}_3$
  - 2 cm³ of bladder: $< 90 \text{ Gy}_3$
  - High risk CTV & $D_{90}$: greater than the PD $V_{100} > 90\%$
Radiobiological modelling of doses:

- **Standard brachytherapy dose-rate** – 50cGy/hr
  - Calculate the biologically weighted dose for brachytherapy

- **Standard external beam radiotherapy** is 200cGy/Fr
  - Calculate the biologically weighted dose for external beam

- **Add both together to get the Total Biologically weighted Dose** for tumor & OAR
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Potter, Radiat & Oncol, 78, 2006
Image Based Brachytherapy

Kirisits, Int J. Rad Oncol Biol Phy 65,2 2006
**Image Based Brachytherapy**

- **Situations requiring combined I/C & I/S**
  - Unilateral tumor extension exceeding
    - 3.5 cm at level of ring
    - 2.5 cm at level of pt A
    - 2.2 cm at a distance 3-4cm cranial to ring surface
  - Tumor extension cannot be covered by symmetrical dose distribution of tandem alone without exceeding dose limits for OAR
  - Tumor extension to lower vagina, close to pelvic side wall, posteriorly along ant rectal wall
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**BALANCE**

3-D Image Based Dose volume relations in OAR : tolerable effects

3-D Image Based Dose volume relations in HR/IR CTV : control of disease
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Conclusion

- It is expected that the therapeutic ratio including target coverage & sparing of OARs can be significantly improved, if radiation dose is prescribed to a 3D image-based CTV taking into account dose volume constraints for OARs.

- However, prospective use of these recommendations in the clinical context is warranted, to further explore & develop the potential of 3D image-based cervix cancer brachytherapy.