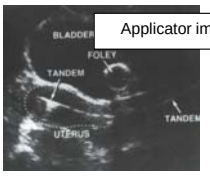
Clinical uncertainties: what is the magnitude?

BrachyNext
Miami 2014

Kari Tanderup

Aarhus University Hospital

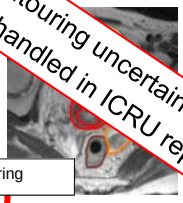
The 6 steps of 3D image guided brachytherapy



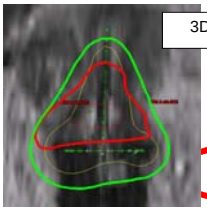
Applicator implant

3D imaging

Contouring uncertainties not yet handled in ICRU reports

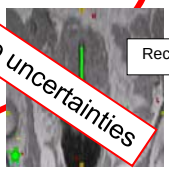


Contouring



3D dose planning

Set-up uncertainties



Reconstruction of applicator

Set-up uncertainties

Dose delivery

Organ/applicator movement

Important publications!

- **Radiotherapy and Oncology 107 (April 2013):**
  - **Special issue on uncertainties in brachytherapy (mainly gyn)**
  - **16 original papers (contouring, inter-fraction, intra-fraction, applicator, vagina dose reporting)**
  - **1 editorial**

- **Radiotherapy and Oncology**
  - **Kirisits C**, Rivard MJ, Baltas D, Ballester F, De Brabandere M, van der Laarse R, Niatsetski Y, Papagiannis P, Hellebust TP, Perez-Calatayud J, Tanderup K, Venselaar JL, Siebert FA. **Review of clinical brachytherapy uncertainties: Analysis guidelines of GEC-ESTRO and the AAPM**. Radiother Oncol. In press

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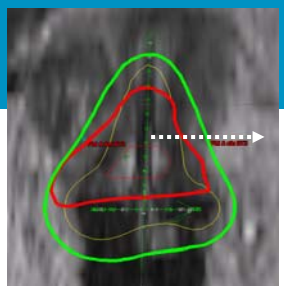
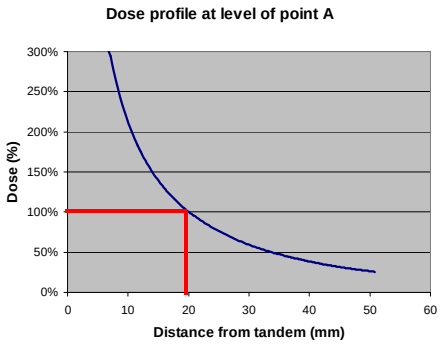
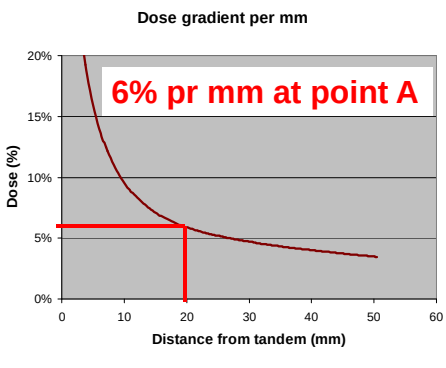
Uncertainties in the high gradient BT dose distribution



Radial dose profile





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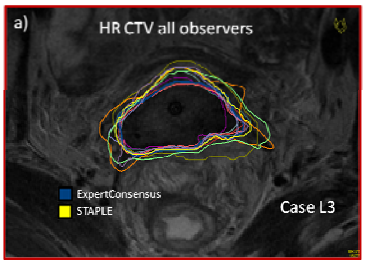
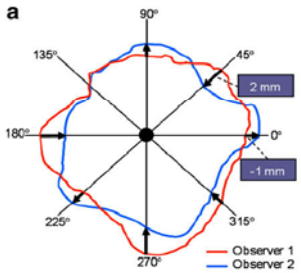
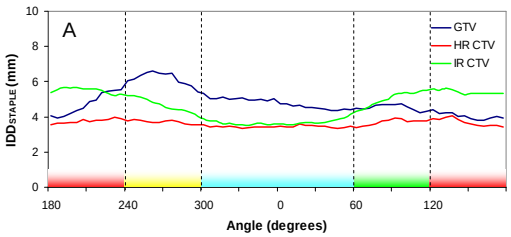
Contouring uncertainties HR-CTV on MRI

- **HR CTV:**
  - **Mean deviation <4mm**
- **GTV, IR CTV:**
  - **Mean deviation <6-7mm**



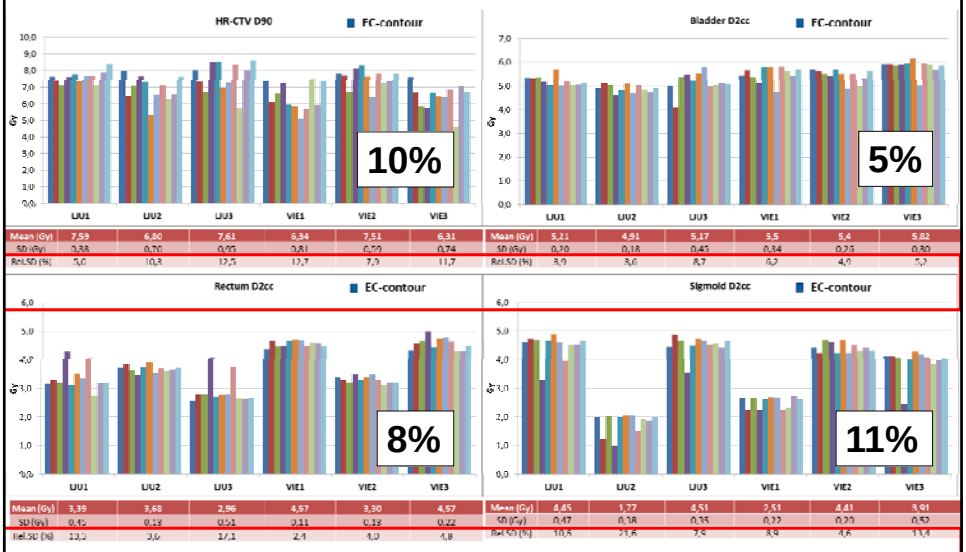




Petric et al, R&O 2008

Petric et al, RO Vol 107, April 2013

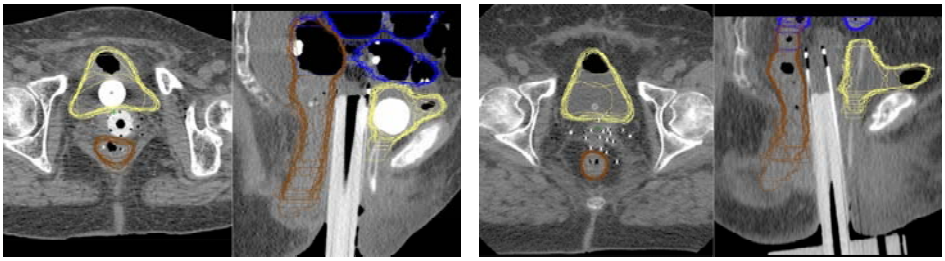
Impact of contouring uncertainties (MRI) on dose



Hellebust et al, Vol 107, April 2013

Contouring uncertainties on CT (interstitial brachytherapy)

Organ	Coefficient of variance
Bladder	16% ± 10%
Rectum	7% ± 2%
Sigmoid	34% ± 19%



Damato et al, IJROBP in press

Reconstruction uncertainties
MRI based intracavitary/interstitial brachytherapy

Reconstruction uncertainties in mm (SD):

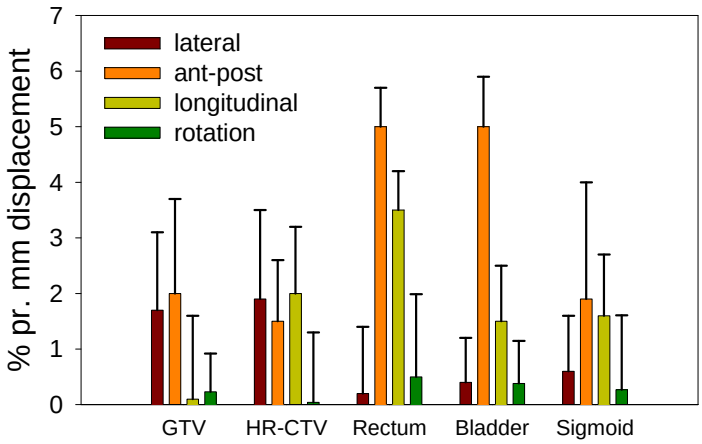
~ 0.5mm in lateral and ant-post directions

~ 1-2mm in longitudinal directions

	Longitudinal SD (mm)	**Lateral** SD (mm)	**Ant-posterior** SD (mm)	**Rotation** SD (mm)
Ring (plastic)	1.4	0.6	0.4	1.2
Tandem (plastic)	1.7	0.6	0.5	-
Titanium Needle	2.2	0.4	0.3	-

S Haack et al., Radiother Oncol 2009

Impact of reconstruction uncertainties on DVH parameters



K Tanderup et al., Radiother Oncol, 2008

Evaluation of needle displacement over 2 days Prostate HDR implantation

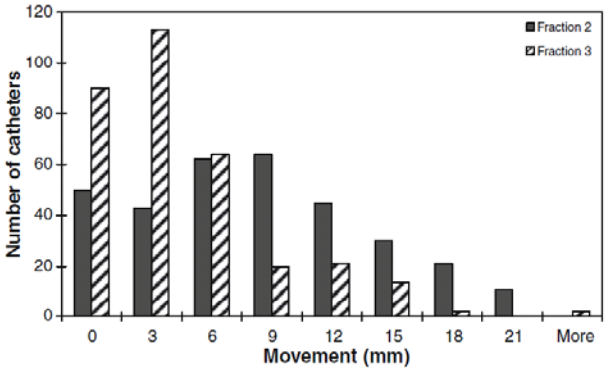
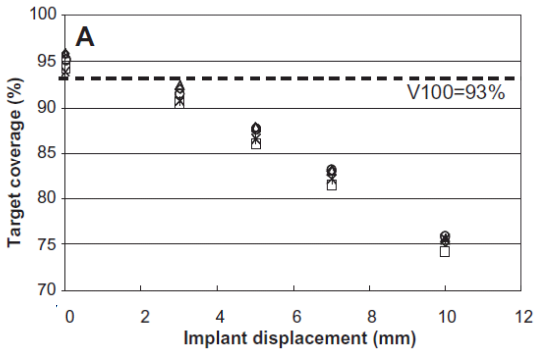


Fig. 1. Frequency histograms displaying the caudal movement in mm of each catheter at fractions 2 and 3 (326 in total).

Simnor, RO 2009

Impact of needle movement

- **Needle movement has significant impact on target coverage**

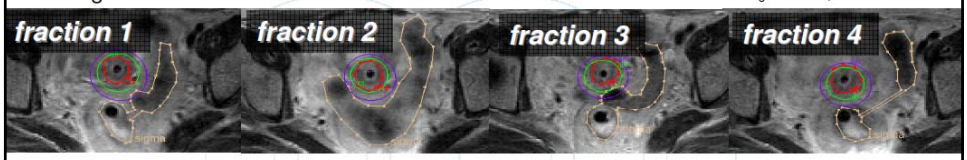


Kolkman-Duerloo, RO 2011

Random dosimetric variations during Brachtherapy

Same plan used for 4 fractions, anatomical changes between irradiations may lead to large random dosimetric uncertainties

Lang et al. 2013, Radiother Oncol



Results of a multicentre study between 6 centres with different treatment/ application techniques (Nesvacil et al. 2013, Radiother Oncol 107 and references therein) :

De Leeuw et al.; Hellebust et al.; Anderson et al.; Mohamed et al.; Lang et al.; Jamema et al.

			Bladder SD D2cc			Rectum SD D2cc			Sigmoid SD D2cc			HR CTV SD D90
total	2.7	1.5	20.3%	4.5	4.1	22.0%	1.6	-0.9	26.8%	-1.1	-1.7	13.1%
Intraaplication	1.3	1.5	17.7	3.8	2.3	20.5	-2.3	-3.7	23.5	-2.5	-4.3	10.8
interapplication	3.9	0.0	22.3	5.8	5.2	23.2	6.8	3.7	30.2	0.4	-0.8	15.1

Note: Changes correspond to physical dose change between 2 time points during course of BT. Effect on total EQD2 (EBRT+BT) depends on fractionation schedule (PDR, HDR, …)

Courtesy Nicole Nesvacil

Uncertainty budget GYN

Table 1
Uncertainty budget (SD) for one intracavitary brachytherapy fraction. The overall uncertainty for the entire treatment course is depending on the fractionation schedule and level of verification.

	Target (HR CTV D90)	OARs (D_{2cm^3})
Source strength	2%	2%
Dose and DVH calculation	3%	3%
Dwell position uncertainty (reconstruction and source positioning)	4%	4%
DVH addition across fractions (previously called "worst case assumption")	NA	1%[a]–7%
Contouring (inter-observer)	9%	5–11%
Intra- and inter-fraction (intra-application) uncertainties[b] (5)	11%	20–25%
Total[c]	12%	21–26%

[a] For the bladder and likely rectum, whereas it has not been evaluated for sigmoid.
[b] Per se including intra-and inter-observer contouring variations.
[c] Contouring uncertainties included through intra- and inter-fraction uncertainties.

Tanderup et al, RO Vol 107, 2013

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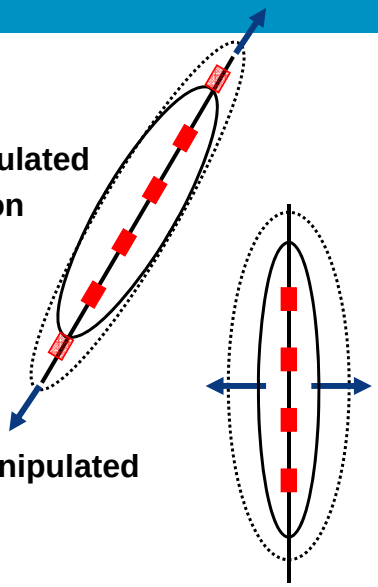
Gradients in brachytherapy

- **Longitudinal direction**
  - **Gradients can be manipulated**
  - **Dependent on application**
- **Radial direction**
  - **Gradients cannot be manipulated**



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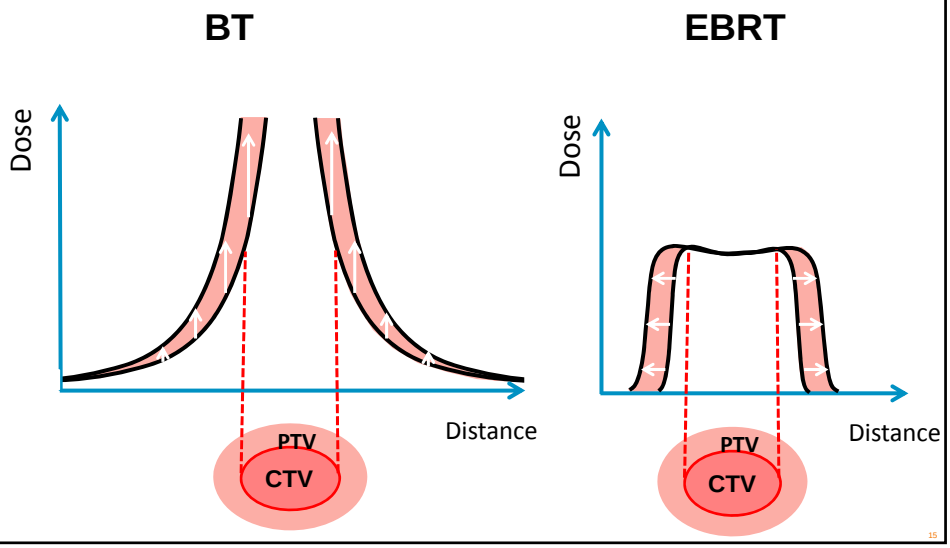
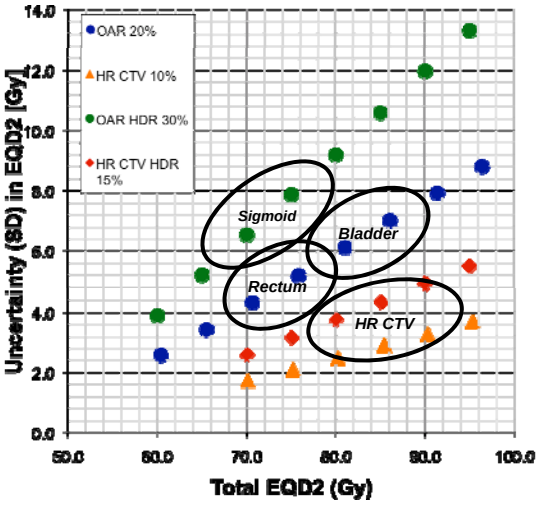
PTV margins in lateral direction?



Impact of uncertainties on total dose

OAR
6-8 Gy (SD)

HR CTV
2-5 Gy (SD)



Examples total dose and uncertainty

- **HR CTV:** D90 = 90 ± 4Gy
- **Bladder:** D_{2cm3} = 85 ± 7Gy
- **Rectum:** D_{2cm3} = 70 ± 4Gy
- **Sigmoid:** D_{2cm3} = 70 ± 7Gy

IS THIS OK?

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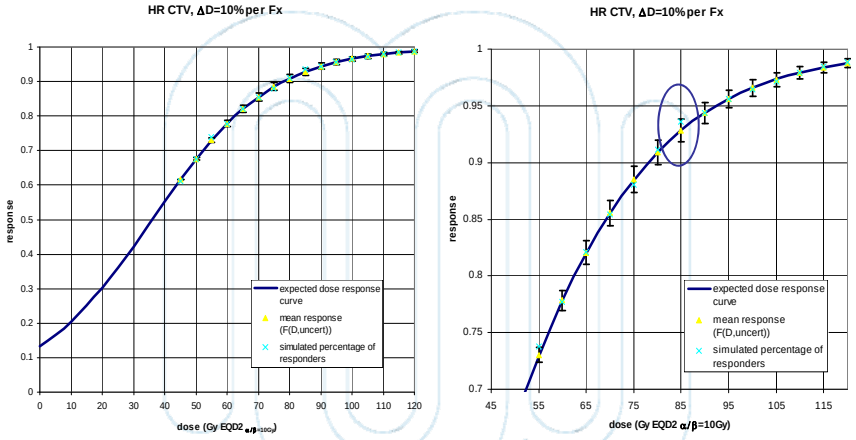
Simulating dose-response curves for HR CTV D90

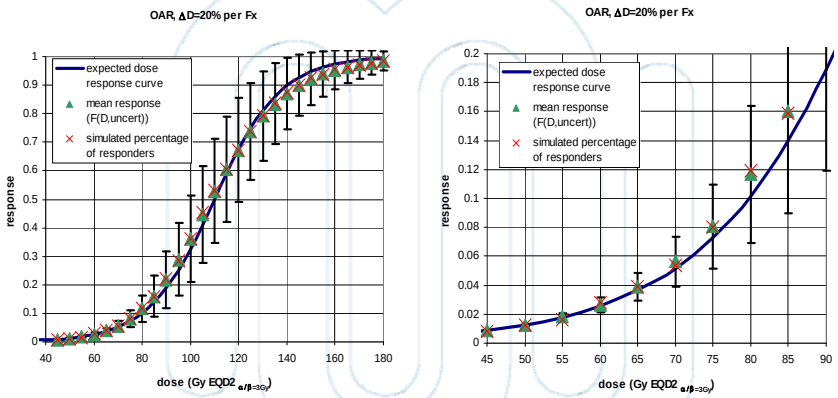


Simulated data with **10%** uncertainty (SD per BT fraction, for EBRT+4xHDR BT).
Error bars: +/-1SD of response probabilities calculated for Individual patients

Negligible systematic differences between simulated „observed" curve and assumed dose-response curve.
Ranges of response probability uncertainties around 85Gy EQD2 are around **2.5%** for individual patients (1 SD of all simulated values (n=10000)).

Courtesy Nicole Nesvacil

Simulating dose-response curves for OAR

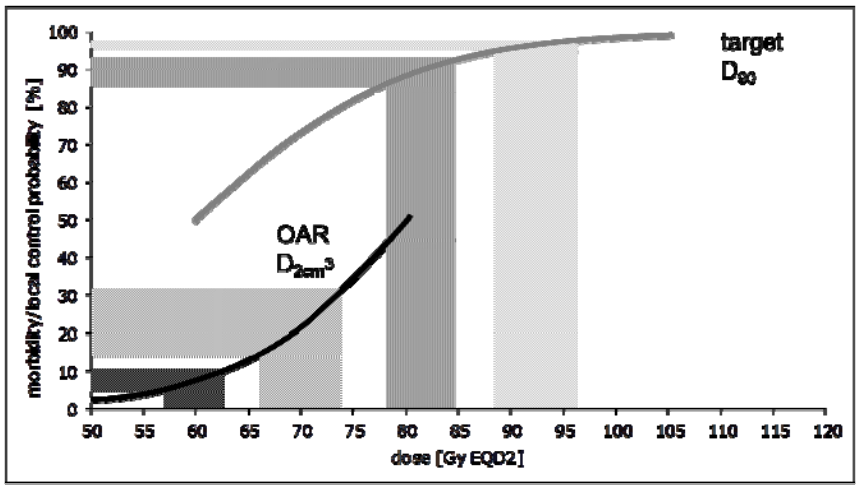


Simulated data with **20%** uncertainty (SD per BT fraction, for EBRT+4xHDR BT).
Error bars: +/-1SD of response probabilities calculated for Individual patients

-Small systematic offset around rectum dose constraint of 70-75Gy
-Range of response probability uncertainty for individual patients **~4-6%**

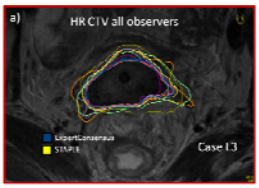
Courtesy Nicole Nesvacil

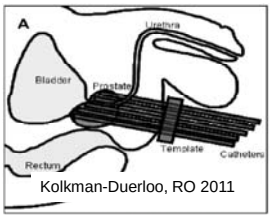
Dosimetric margin



Interventions to decrease uncertainties

- Target
  - Contouring training
    - ESTRO contouring workshops
  - Re-imaging for assessment of catheter position (interstitial)
- OARs
  - Re-imaging
  - Re-planning
- What do we need?
  - Tools for quick plan adaptation
  - Alternative imaging modalities (CBCT, US)





Kolkman-Duerloo, RO 2011

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Conclusion

- Major clinical uncertainties are related to:
  - Contouring
  - Needle movement
  - Organ movement
- Geometrical PTV margins are not generally applicable for brachytherapy
- In brachytherapy ”dosimetric margins” may be the ”secret of success” even in the presence of considerable uncertainties

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