

General Clinical Applications of Brachytherapy Physics



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Learning Objectives

1. Consider the physical aspects of brachytherapy.
2. Understand the physical limitations in clinical applications of brachytherapy.
3. Know some of the emerging developments in the physical aspects of clinical applications in brachytherapy.

Conflicts of Interest

This presenter has no known conflicts regarding this presentation.

Brachytherapy

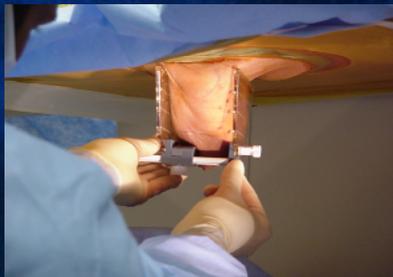
- Brachytherapy was the original IMRT, delivering very conformal radiation to a target while preserving neighboring structures.
- With differential source strength, dwell time or source placement, dose distributions can be finely controlled.
- Most brachytherapy has been image guided for decades.

Clinical Application Example

Breast Brachytherapy

Interstitial Breast Brachytherapy

Mammographic Template Guided

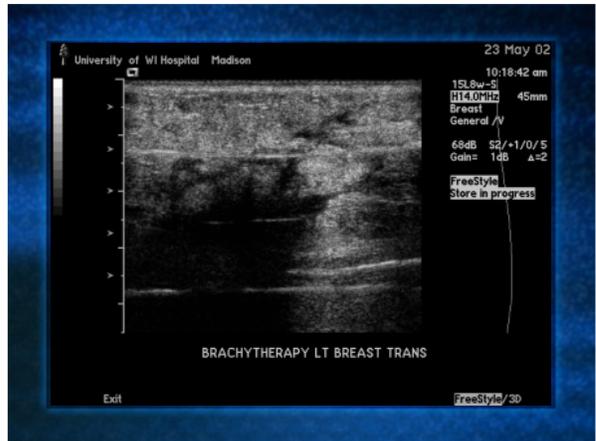
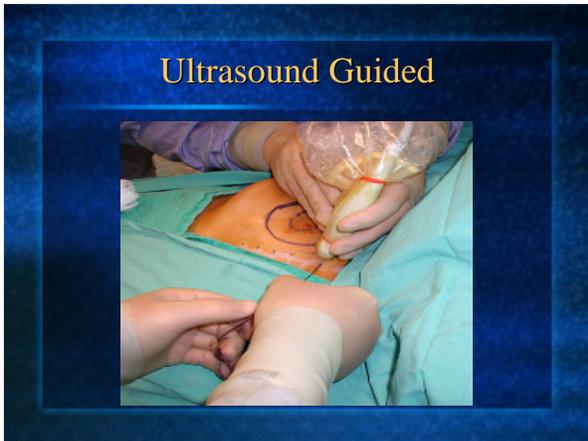


Target Volume Definition



Target Volume

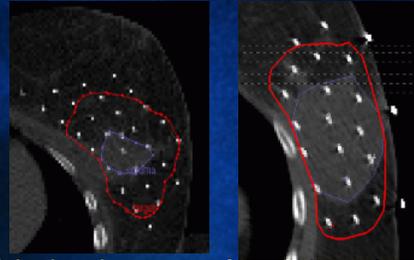
Lumpectomy
cavity/surgical
clips + 2-cm
margin



Other Approaches

- Supine, CT guided, freehand
- Supine, CT-template guided
- Yet to see MR guided

Target Limitation



Bringing the target of the skin and pecs

Manual Reoptimization

Org	Vol	Mean	Max
7	2	4	30.9
8	2	5	30.1
9	2	5	30.1
10	2	2	30.8
11	2	8	31.2
12	2	2	30.8
13	2	3	30.8
14	2	4	30.8
15	2	5	30.8
16	2	5	30.8
17	2	2	31.4
18	2	8	31.4
19	2	8	31.2

Org	Vol	Mean	Max
7	2	4	33.0
8	2	5	31.8
9	2	5	33.2
10	2	2	33.2
11	2	8	33.2
12	2	2	33.2
13	2	3	33.2
14	2	4	33.2
15	2	5	33.2
16	2	5	33.2
17	2	2	33.2
18	2	8	33.2
19	2	8	33.2

Analysis of Interstitial Implants

- $PTV_{100} > 98\%$.
- 150% isodose surfaces do not coalesce.
- HI typically about 0.8
- Skin < 100%.

Prescribed Dose

10 fx of 3.4 Gy (34 Gy)
for $BED_{Gy10}=45.6$

Intracavitary Breast Brachytherapy

MammoSite® RTS Device

Spherical

- 4-5 cm sphere
- 5-6 cm sphere

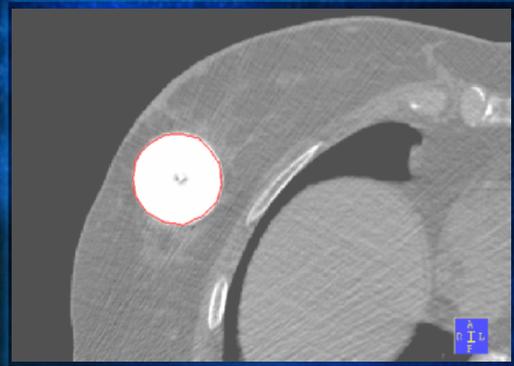


Ellipsoidal

- 4 X 6 cm ellipse
- 4 X 8 cm ellipse
- 5 X 9 cm ellipse



Courtesy of Jeffrey A Dorton, Proxima Therapeutics, Inc.



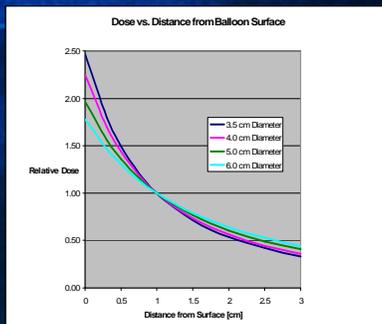
Patient Selection

- Small tumors ≤ 1.5 cm diameter
- Roundish cavity
- Inserted during or soon after tyelectomy

Prescription Location

The prescribed dose is delivered to 1 cm beyond the balloon surface.

MammoSite Depth Dose



MammoSite Homogeneity

Balloon Diameter	Ideal Homogeneity Index
3.5 cm	0.61
4.0 cm	0.65
5.0 cm	0.72
6.0 cm	0.79

Procedure

- Placement: Often by surgeon – could be by radiation oncologist.
- Localization: CT is necessary (we will see why).
- Dosimetry: Takes little time. (A little longer if more than one dwell position used.)

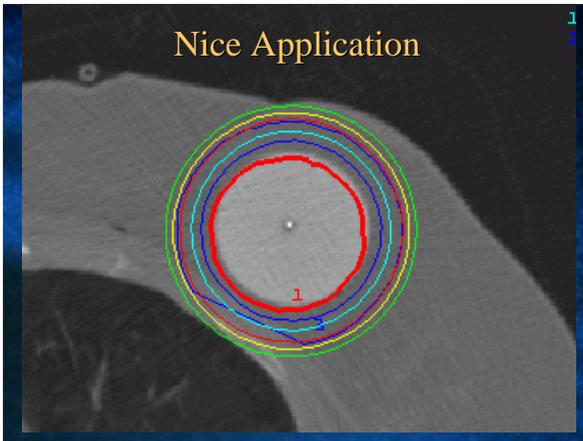
Planning Criterion 1

Applicator should be at least 1 cm away from the skin.

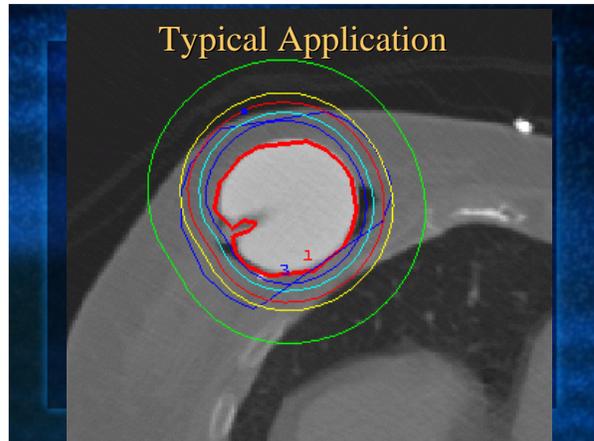
- Acceptable as close to skin as 0.6 cm.
- Skin *will* exceed 100%.
- Skin *should not* exceed 150%.

Example: (radius to PD/radius to skin at 0.6 cm)²
= (3.0 cm / 2.6 cm)² = 1.33 => Skin dose = 133%.

Nice Application

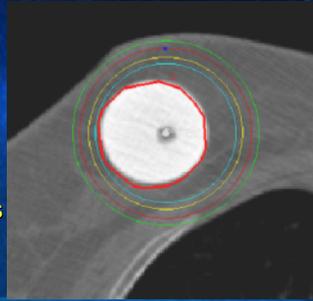


Typical Application

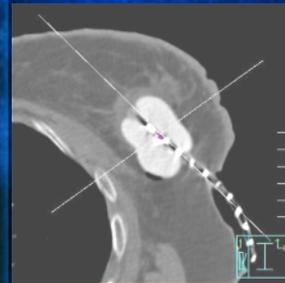


Planning Criterion 2

Source should be centered with respect to the applicator (except when avoiding the skin if balloon is too close.)



Planning Criterion 3: Balloon Shape



Inappropriate Balloon Selection

Courtesy of Jeffrey A Dorton
Proxima Therapeutics, Inc.

Addressing these Problems

- The skin proximity and the shape of the cavity are irrelevant for interstitial implants.
- Proposition: having multiple source paths in an intracavitary application may give more control of the dose distribution and overcome these limitations.

SAVI



•Picture courtesy of Robert Kuske

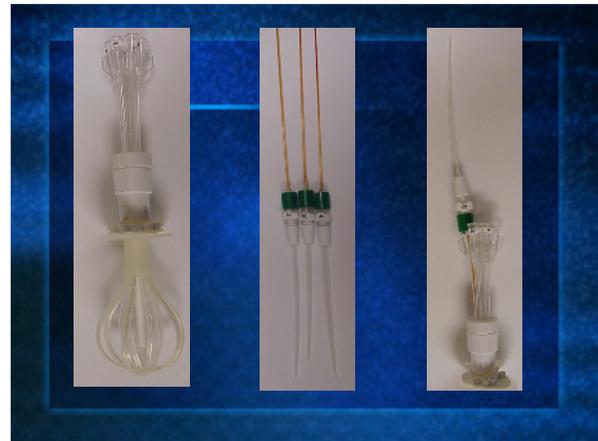
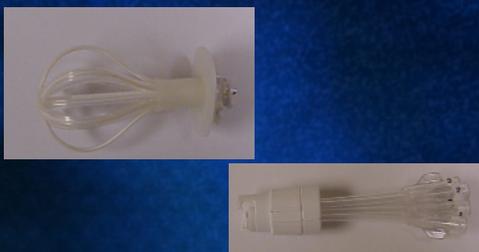
SAVI Concerns

- Air in the cavity – may affect the doses by 6-8% (Richardson; ABS 2008)
- Source paths in contact with the tissue.

ClearPath



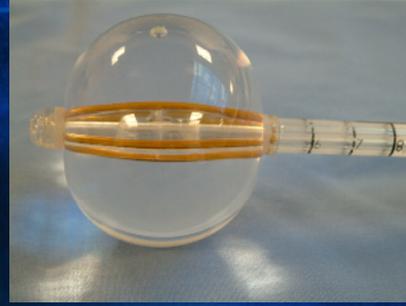
ClearPath



ClearPath Concerns

- Air in the cavity – may affect the doses by 6-8%.
- Control on the positions of the source paths.

Contura



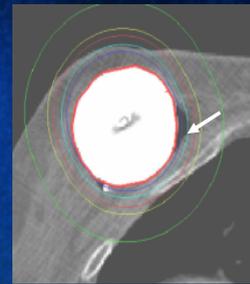
Slide courtesy of Dorin Todor

Some Dose Steering



Planning Criterion 4: Be wary of voids!

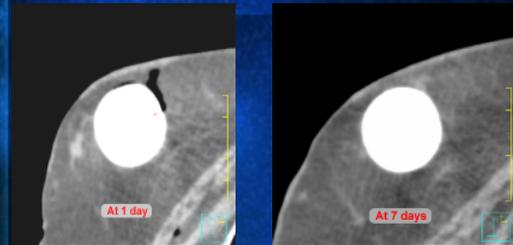
They push the target tissue away from the source.



However...

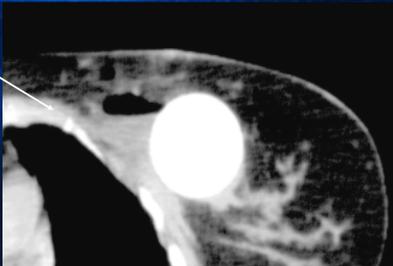
- These treatments are intracavitary. The dose falls continually from the surface, but not abruptly.
- While the edge of the tissue beyond the air pocket may not receive 95%, or 90%, of the dose, it may be receiving just 5% less than that.
- That maybe enough.
- We don't have enough information yet to judge.

Air Gap Resolution



Images Courtesy of Jeffrey A Dorton
Proxima Therapeutics, Inc.

Air/Fluid level

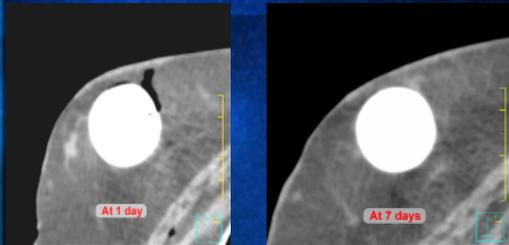


Courtesy of Jeffrey A Dorton Proxima Therapeutics, Inc.

Air Pocket Resolution

- The air pockets fill with fluid, rather than deflate.
- The tissue does not move back.
- Most of the time.

Air Gap Resolution?



Images Courtesy of Jeffrey A Dorton Proxima Therapeutics, Inc.

Treatment Planning

Obviously requires CT
treatment planning. Maybe
MRI.

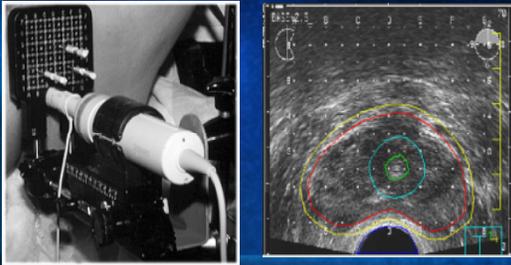
Comparison of APBI Techniques

- Interstitial gives better control over the dose distribution
 - Requires more time and skill
 - Conformance to target
 - Shape of target is unimportant
 - Protection of skin, lung, pecs, body
- Intracavitary brachytherapy
 - Requires less skill
 - Has simpler dosimetry, easier dosimetry
 - Mostly will be on target, except with voids
 - Gives higher doses to surroundings, such as skin and ribs

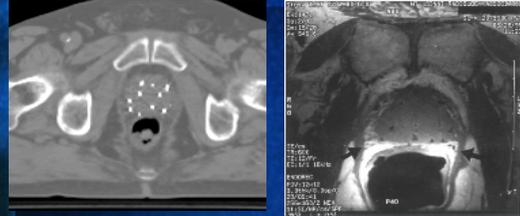
Clinical Application Example

Prostate Brachytherapy

Prostate Implant Template with Ultra-sound Probe

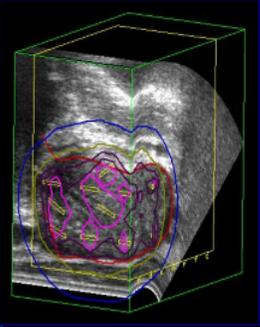


CT and MR of a Prostate Implant



MR shows the anatomy much better, but the axial location is poorly defined and the prostate shape distorted by probe.

Live-time, 3-D Ultrasound Guided Prostate Implant



- Optimize in the OR
- Mark sources as dropped
- Recalculate and reoptimize

ABS nomenclature for different types of prostate brachytherapy planning

Planning approach	Definition
Preplanning	Creation of a plan outside the operating room (OR) hours, days or weeks before the implant procedure.
Intraoperative	Plan created in the OR. The patient remains stationary between the time of the volume study and the implant procedure.
Interactive	The treatment plan is revised periodically during the implant procedure using image-based feedback of needle position to recalculate dose.
Dynamic dose calculation	Dose distribution continuously updated using deposited seed position feedback.

Slide from Wayne Butler

Why not Plan before the OR

- Patient inconvenience (although, wouldn't you rather be inconvenienced if it could give a better result?)
- Prostates often change between study and procedure.
- CT is not the best at evaluating the size of the prostate.
- For planned cases, much of the time is taken duplicating the position for the study.

Why plan prior to the OR?

- Cost effective
 - Dosimetry time is cheaper than OR time
 - Less seed waste
- Better dosimetry
 - All team members have deliberate input
 - Optimum plan is rarely done on first try
- Intraoperative planning remains an option

Slide from Wayne Butler

Mick applicator vs. pre-loaded needles

- Mick applicator
 - Unlimited flexibility in seed placement along the needle track
 - More time consuming than preloaded
 - Every seed must be placed individually
- Pre-loaded needles
 - Difficult to deviate from the plan
 - Shorter OR time if loaded pre-operatively
- No evidence yet for a difference in outcomes between the two approaches

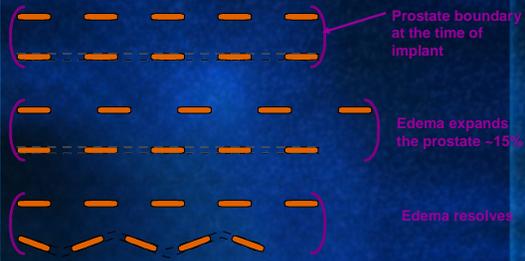
Slide from Wayne Butler

Loose seeds vs. stranded seeds

- Loose seeds
 - Move with the surrounding tissue to minimize the effect of edema and its resolution
 - May move significant distance from intended location or be lost to dosimetry
- Stranded seeds
 - Lower probability of loss although may lose whole strand
 - Easier to find post operatively
 - More expensive, difficult to calibrate
- No convincing evidence of better dosimetry with one approach over another

Slide mostly from Wayne Butler

Loose seeds versus stranded seeds



Slide from Wayne Butler

Use of third-party seed loading and source calibration services

- Convenient, time-saving
- Radiopharmacy assay of seeds does not remove your responsibility to assay
- TG 40, 56, and 64 guidelines remain
 - Assay 10 % of order or 10 seeds, whichever is greater
 - Mean assay should agree with manufacturer's certificate to $\pm 5\%$ or else act to resolve discrepancy
 - With sterile source assemblies, either order > 1 loose source for assay or assay 10 % of assemblies using sterile well chamber inserts

Slide from Wayne Butler

Seed and needle placement approaches

- Nomogram approaches
 - 75% of volume determined seed strength to be placed on the periphery
- Uniform loading
 - Initial Seattle approach assumed little cumulative dosimetric effects from very low energy seeds
- Modified uniform/peripheral loading
 - Basis of most manual planning
- Peripheral loading
 - Assumes significant long-range cumulative dose effects: most appropriate for HDR

Slide from Wayne Butler

Sources for Permanent Interstitial Implants

Material	Avg. Photon Energy [keV]	Half life [days]	HVL Pb [mm]
(Radon)	830	3.83	12
Au-198	412	2.70	3
I-125	27	60	0.025
Pd-103	21	17	0.008
Cs-131	30	9.7	~0.04

A Little Prostate Biology

- Prostate cancers grow slowly
- Few cells will be in the sensitive parts of the cell cycle at any given time.
- Therefore, the conventional thought was, it would be good to carry therapy over a long period.
- Thus came about the use of ^{125}I with its 60 d half-life.

A Little Prostate Biology

- For aggressive tumors (more quickly growing) some people use ^{103}Pd .
- Interestingly, some practitioners use ^{103}Pd for all tumors, and don't seem to have any worse results.

A Little New Prostate Biology

- New studies are showing that prostate cancer has a low α/β , about 1.5 - 2.
- Low α/β ratios indicate that for the most damage, small large fractions should be used,
- Or the dose delivered in a short time (Shorter than with ^{103}Pd , for example with ^{131}Cs)
- Possibilities? Just external beam or implants with ^{198}Au .

Cs-131

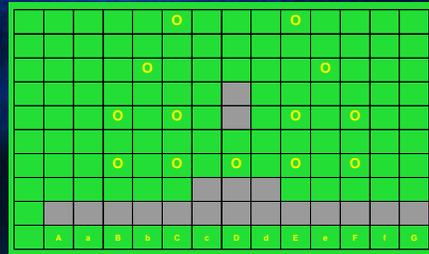
- Mean photon energy ~ 29 keV
 - I-125 ~ 27 keV; Pd-103 ~ 22 keV
 - Radial dose function falls off more gradually than I-125 and Pd-103
- Half life = 9.7 days
 - Initial dose rate to deliver total dose of 100 — 120 Gy is 7.15 – 8.58 Gy/day
 - Acute reactions more likely
- Potential radiobiological advantage, particularly for aggressive cancers
- 16% dose rate constant uncertainty
 - 0.915 cGy/h/U at Univ. Washington
 - 1.062 cGy/h/U at Yale

Slide mostly from Wayne Butler

HDR Prostate Brachytherapy

- Should be good for the low α/β
- Similar in approach to LDR
- Fractionated either BID or QIW
- Planned and "Optimized" on the spot

Template Design



Standard but Flexible Template Pattern
Fewer tracks than LDR

Slide from Eric Hendee

One Sample HDR Fractionation Schedule of Many

- 4.4 cGy x 4 Fx
- 2 first day (noon and 5:30)
- 2 second day (8am and 2pm)
- External beam = 23 x 2 Gy
- $BED_{Gy2}=148$

Temporary LDR for Prostate Treatment

- Lower α/β tumor of 1.5 Gy than normal tissue of 3 Gy prefers hypofractionated HDR (>2 Gy per fx)
- Slower tumor repair at 4 hour than normal tissue at 1.5 hour prefers LDR
- Temporary LDR would maximize the benefits of each
- *More efficient towards tumor response than late complications*

NTD, tumors and normal tissues	Temp LDR (40.3 Gy in 42 fx)	HDR (9.5 Gy by 4 fx)	Permanent 145 Gy ¹²⁵ I	Permanent 125 Gy ¹⁰³ Pd
tumor response	127.2 Gy	119.4 Gy	79.0 Gy	97.4 Gy
late complications	86.0 Gy	95.0 Gy	91.4 Gy	86.5 Gy
therapeutic ratio (TR)	2.27	1.26	0.86	1.13

Slide mostly from Liyong Lin

Brachytherapy vs. Photon and Proton XRT

Risk Group (> 100 patients/group)	Brachytherapy 8-10 yr bNED Top 5 reports	IMRT 8 yr bNED MSKCC	Proton [#] 8 yr bNED Loma Linda
Low	90 – 98 %	89 %	< 90 %
Intermediate	88 – 96 %	76 %	< 81 %
High	78 – 88 % *	67 %	< 62 %

* Combined with photon XRT

[#] Some photon therapy added. Results not reported by risk group

Slide from Wayne Butler

Clinical Application Example

3-D, Intracavitary Cervical Brachytherapy

Reasons to Move to Volume-image Guidance

- We have come to expect to prescribe treatments based on target volumes
- Radiographic imaging fails to delineate soft tissues -either target or organs at risk.
- Thus only with volume imaging can we assess or control treatments with the control we are use to in external-beam radiotherapy.

Intracavitary Dose Specification

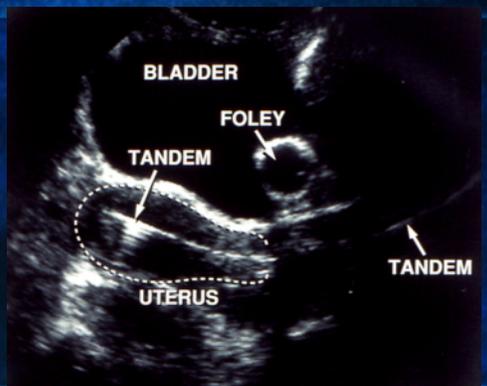
- Volume dose specification may not be appropriate.
- Treatment experience based on a dose fall-off, and that dose beyond the target may be essential to treatment success, as might be the very high dose near the appliance.

Radiographic and Fluoroscopic Imaging

- Most accurate modality for source localization
- Readily available
- Cannot image target
- Hey, it cannot image the normal structures either
(can try to use surrogates, such as a Foley, but that does not indicate most of the organs at risk)

Ultrasound

- Can be very useful during tandem insertion
 - Localizing the cervical canal when obscured by tumor,
 - detecting a retroverted uterus before tandem insertion.
- Also very helpful in assessing the uterine wall thickness for placement of optimization points for endometrial cancer (but this is a different, although equally interesting topic).

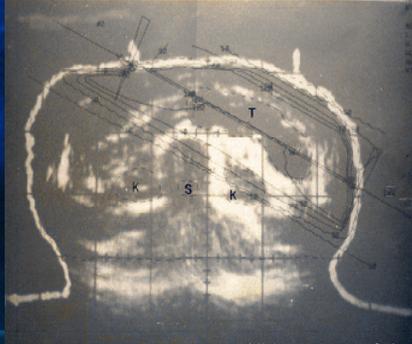


Slide courtesy of Daniel Peterit

US Treatment Planning

- The US used in cervical localization normally is freehand, so does not produce a volume image.
- US systems can create volume images by
 - Sequential cuts, such as in prostate brachytherapy, but this requires stepping the probe in a rigid holder, of
 - Sweeping the beam through a volume.
- Thus, it cannot be used for treatment planning
- *IF* we went back to the old B-scanners, we could.

Old Ultrasound in Treatment Planning



Slide courtesy of Jim Zagzebski

US Treatment Planning - 2

- US would also have a very difficult time imaging source-simulating markers in an applicator.
- US compatible applicators would have to be developed.

Computed Tomography

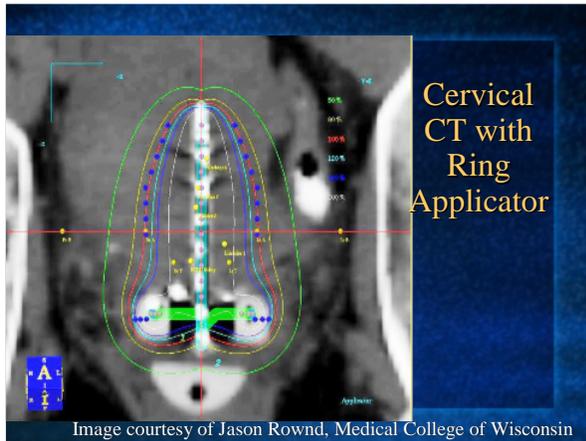
CT is the obvious candidate for volume-imaged based treatment planning for cervical intracavitary brachytherapy.

- Long experience in treatment planning for external beam.
- Fairly good soft-tissue contrast, visualizing bladder and rectum.
- The images are radiological quantities used in dose calculations.
- Often readily available in radiotherapy departments or nearby.

CT Treatment Planning - 2

Problems with CT treatment planning for Cx TP:

1. Requires special applicators.
2. Requires moving the patient after localization to the treatment room
3. CT fails to provide differentiation between the uterus, periuterine tissues and tumor.
4. Localizing the sources



CT Treatment Planning - Summary

CT treatment planning for cervical intracavitary brachytherapy has been done (since Schoepple et al, 1989), and it is a way of determining the doses delivered to organs at risk, but not for tumor dose distribution.

Magnetic Resonance

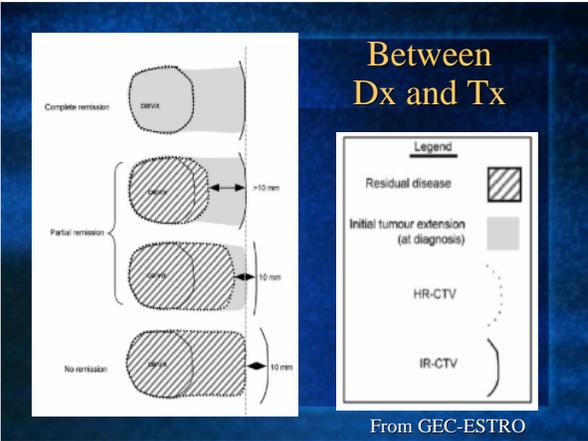
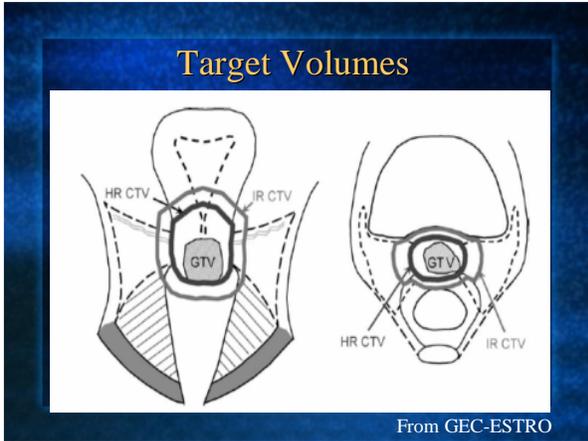
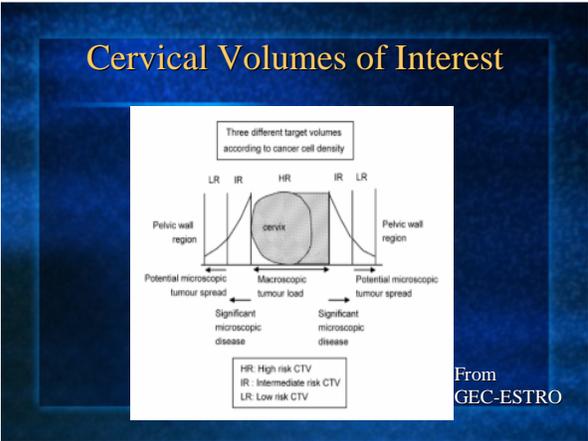
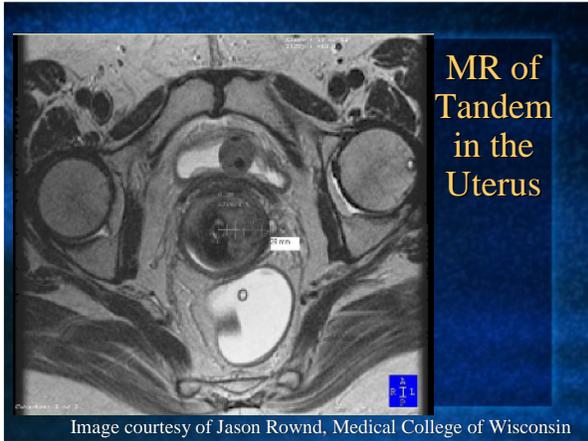
- MR can differentiate between uterus, uterine tumors, and other pelvic tissues, as well as showing the regional organs at risk.
- MR does produce a true volume image.

MR Treatment Planning - 2

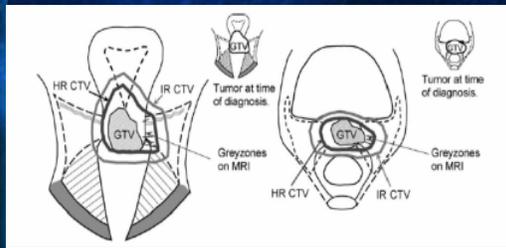
Problems with MR treatment planning for Cx TP (compare with the CT list):

1. Requires special applicators.
2. Requires moving the patient after localization to the treatment room*
3. CT fails to provide differentiation between the uterus, parauterine tissues and tumor.
4. Localizing the sources

*A few facilities have HDR in the MR room.

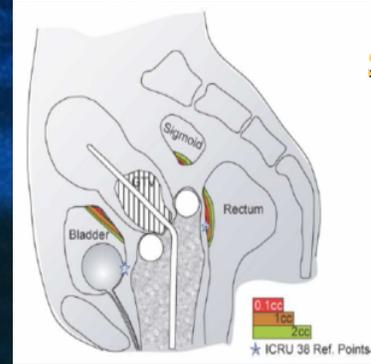


For Extensive Disease



From GEC-ESTRO

Normal Structures



From
GEC-ESTRO

Conclusions

1. Clinical brachytherapy is highly coupled with physics.
2. Most of clinical brachytherapy is changing fairly rapidly.
3. This is a fun time to be doing brachytherapy physics