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.

Limitations

Due to file size limitations for this handout, many of the figures have had to be removed. I apologize for the lack of clarity that results.

Conflicts of Interest

This presenter has no known conflicts regarding this presentation.

Brachytherapy

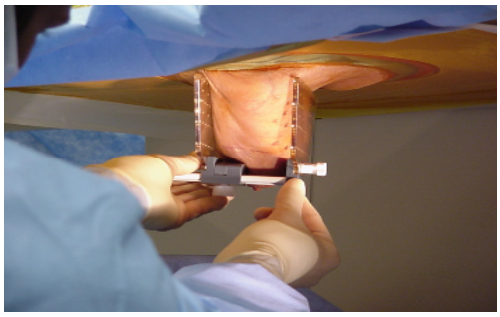
- Brachytherapy was the original IMRT, delivering very conformal radiation to a target while preserving neighboring structures.
- With differential source strength, dwell time or source placement, dose distributions can be finely controlled.
- Most brachytherapy has been image guided for decades.

Clinical Application Example

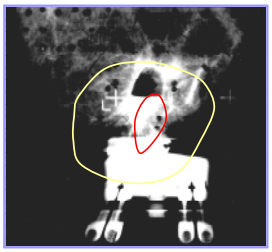
Breast Brachytherapy

Applicator Placement Techniques

- Interstitial:
  - Template-guided prone approach - uses a stereotactic core biopsy table with digital mammographic guidance
  - Free-hand supine approach - uses ultrasound guidance
- Intracavitary: Balloon catheter placed either at the time of tylecomy or soon thereafter.



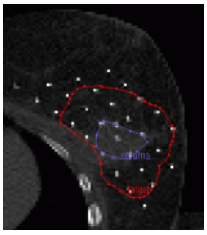
Target Volume Definition

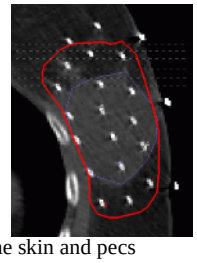


Target Volume

Lumpectomy cavity/surgical clips + 2-cm margin

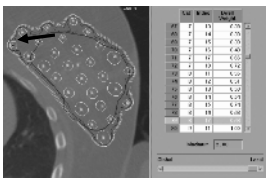
Target Limitation

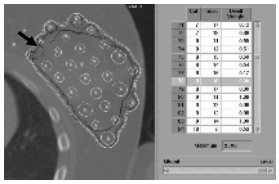




Bringing the target of the skin and pecs

Graphical Optimization





Analysis of Interstitial Implants

- $_{PTV}V_{100}$ > 98%.
- 150% isodose surfaces do not coalesce.
- Skin < 100%.

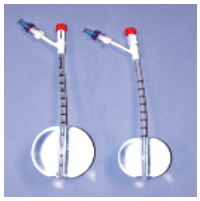
Prescribed Dose

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

Intracavitary Breast Brachytherapy

Two MammoSite® RTS Devices

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



Courtesy of Jeffrey A Dorton
Proxima Therapeutics, Inc.

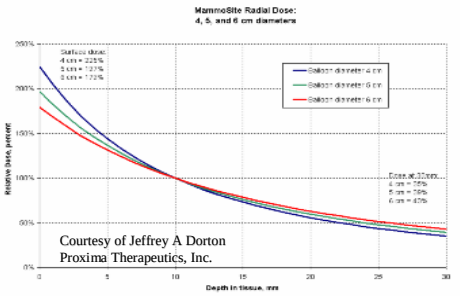
Patient Selection

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

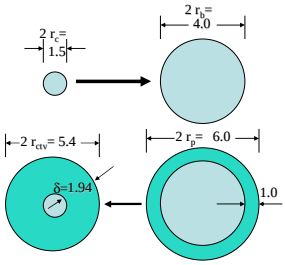
Prescription Location

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

MammoSite Depth Dose



Theory Behind Treatment Volume



- The balloon expands the cavity from 1.5 cm to 4.0 cm.
- The 1 cm margin for the expanded cavity corresponds to an approximately 2 cm margin for the collapsed cavity.

And So

- In theory, the volume of the breast treated is actually quite large.
- In fact, there is little or no stretching, so the effective radius for volume treated is exactly 1 cm beyond the cavity: for a 4 cm balloon, 80 cm^3.

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.)

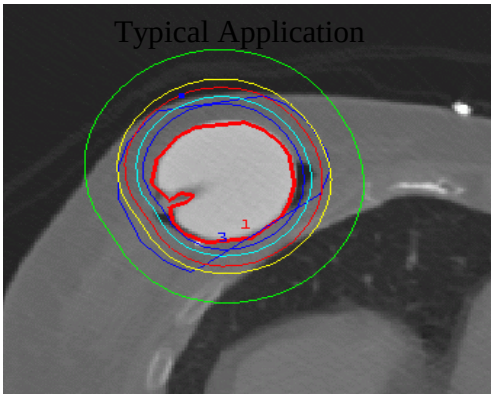
Planning Criterion 1

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%.

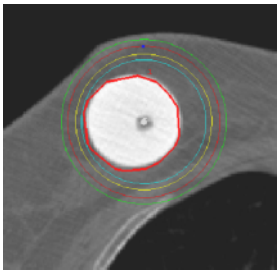
Typical Application

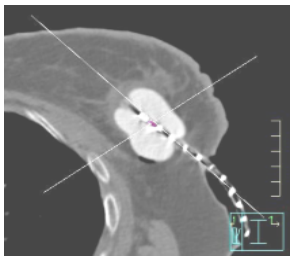


Planning Criterion 2

Source should be centered with respect to the applicator

(except when avoiding the skin if balloon is too close.)





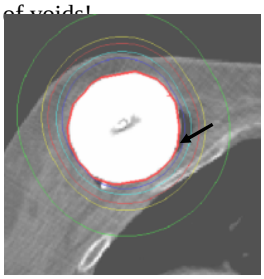
Inappropriate Cavity Selection

Planning Criterion 3: Balloon Shape

Courtesy of Jeffrey A Dorton
Proxima Therapeutics, Inc.

Planning Criterion 4: Be weary of voids!

They push the target tissue away from the source.



Possible Evaluation for Void Significance

- One criterion: $_{PTV}V_{100}$=95%
  - Don't include the volume of the balloon in the PTV.
  - Bubble must < 8 *mm* for a 4 cm balloon.
- Another criterion: $_{PTV}D_{100}$=x% of PD
  - To maintain >95% of PD, the bubble must <0.8 *mm*.
  - To maintain >90%, the bubble must <1.6 *mm*.

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 Pocket Resolution

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

Treatment Planning

Obviously requires CT treatment planning. Maybe MRI.

IMRT for APBI

- IMRT can make a nicely uniform dose distribution in the target, with low doses to the skin, heart and maybe pecs.
- Integral dose likely high because of the number of fields.
- But the big issue is immobilization and reproducibility.
  - Boards don't cut it
  - Molds are better not necessarily okay for PBI
  - Adaptive, image-based RT could be good.

IMRT for APBI - Doses

- The dose distribution for external-beam is much more uniform that for brachytherapy of any type.
- For the same peripheral dose, the EUD is lower.
- This may have a biological effect – we don't know.
- To compensate, protocols call for higher peripheral doses for IMRT APBI.

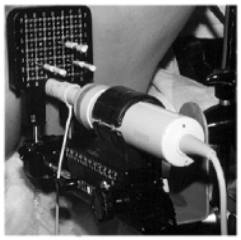
Comparison of APBI Techniques

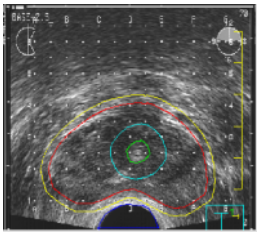
- External-Beam has problems with immobilization and the effective dose is lower for a given prescription dose.
- Interstitial gives better control over the dose distribution
  - Conformance to target
  - Shape of target is unimportant
  - Requires more time and skill
  - Protection of skin, lung, pecs, body
- Intracavitary brachytherapy
  - Mostly will be on target
  - Requires less skill
  - Has simpler dosimetry
  - Gives higher doses to surroundings

Clinical Application Example

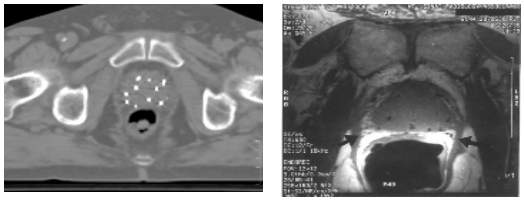
Prostate Brachytherapy

Prostate Implant Template with Ultra-sound Probe

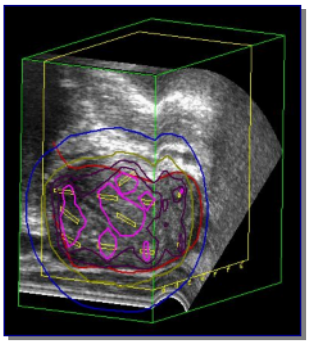




CT and MR of a Prostate Implant



MR shows the anatomy much better, but the axial location 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

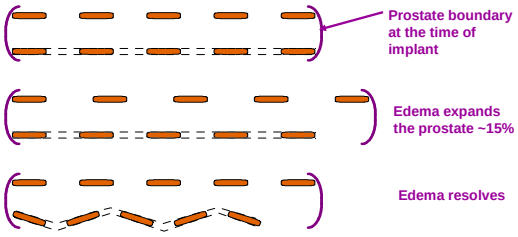
Slide from Wayne Butler

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 ± 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.

New brachytherapy radionuclide: Cs-131

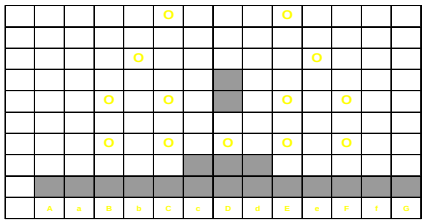
- Mean photon energy ~ 29 keV
  - I-125 ~ 27 keV; Pd-103 ~ 22 keV
  - Radial dose function falls off more gradually than I-125 and Pd-103
- Half life = 9.7 days
  - Initial dose rate to deliver total dose of 100 — 120 Gy is 7.15 – 8.58 Gy/day
  - Acute reactions more likely
- Potential radiobiological 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

- 440 cGy x 4Fx
- 2 first day (noon and 5:30)
- 2 second day (8am and 2pm)

- External beam = 23 x 200 cGy

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 hr)	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	56.0 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 cannel 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).

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.

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, pariuterine 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.

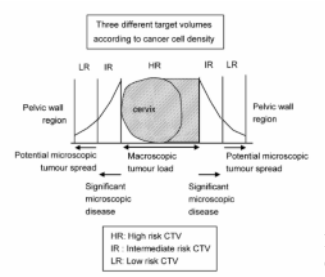
MR Treatment Planning - 2

Problems with MR treatment planning for Cx TP:

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

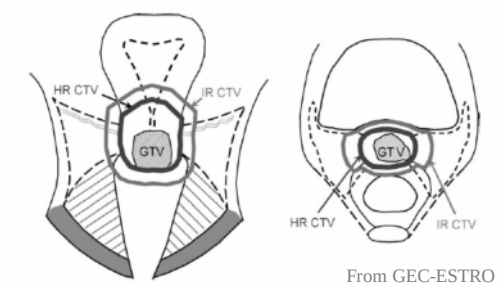
*A few facilities have HDR in the MR room.

Cervical Volumes of Interest



From GEC-ESTRO

Target Volumes



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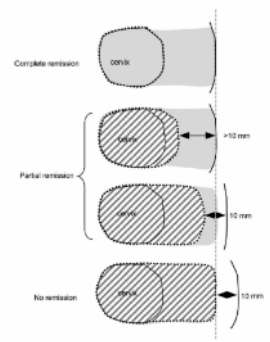
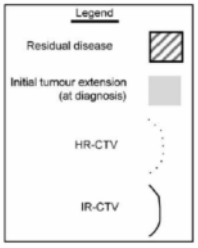
Between Dx and Tx





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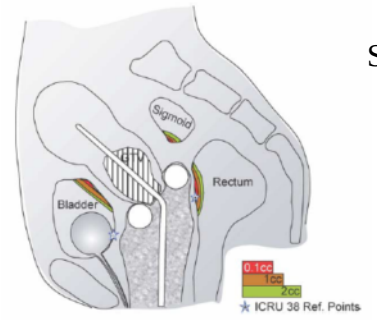
Normal Structures



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