

The Xoft AXXENT™ Electronic Brachytherapy System

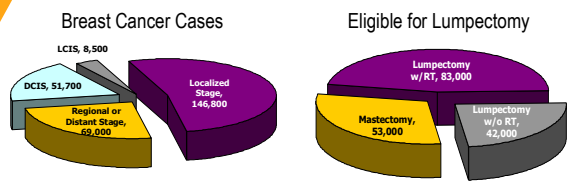
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Science Dept.
Xoft, Inc. Sunnyvale, CA

Outline

- Motivation in the breast market
- Overview of the Axxent™ system
- Patient and treatment-centric comments
- X-ray source characterization and testing
- Some fun source physics
- Future directions and thoughts

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Breast Cancer Cases and Treatments



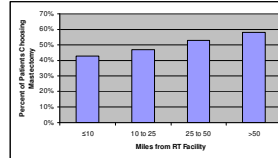
- 276,000 U.S. breast cancer cases in 2006
 - 178,000 eligible for lumpectomy (>60%)
 - Less than half received radiation
 - One quarter opted for mastectomy
 - One quarter skipped radiation therapy

©Combined New Invasive, DCIS, LCIS and Regional
©Combined localized 60% of DCIS patients with unicentric disease
Source: American Cancer Society: Cancer Facts and Figures 2005-6, NCI
SEER Incidence Data, 1998-2002
BCT = Breast Conserving Therapy

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Patient Choices Affected by Access to Therapy

Choice of Mastectomy



Distance and Breast Conserving Therapy Patient Compliance

| Miles Traveled | Number of Patients | % Receiving RT |
|----------------|--------------------|----------------|
| <10 | 621 | 82% |
| 10 to 24 | 158 | 86% |
| 25 to 49 | 76 | 78% |
| 50 to 74.9 | 79 | 69% |
| 75 to 99.9 | 100 | 57% |
| >100 | 88 | 43% |

Mastectomies rates increase markedly for patients living many miles from a radiation therapy center

The further a patient is from a treatment center the poorer their compliance with treatment recommendations

Impact of Patient Distance to Radiation Therapy on Mastectomy Use in Early Stage Breast Cancer Patients, A. Schroten et al., Journal of Clinical Oncology, October 1, 2005
Journal of National Cancer Institute, February 2, 2000 New Mexico Statistics following Breast Conserving Surgery

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Current Treatment Modalities

- External beam
 - 6 to 8 weeks of daily treatments (uggghh)
- Interstitial brachytherapy (isotope based)
- 5 day treatment with HDR Ir-192 (hmmm...)
- ~ 20 needles inserted through breast (arrghhh)
- Balloon brachytherapy (isotope based)
 - Balloon inserted and inflated to fill lumpectomy cavity
 - 5 day treatment with HDR Ir-192
- All of these are done in a highly shielded vault

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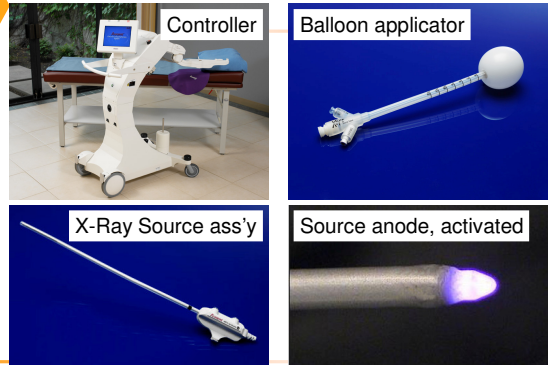
The Xoft Axxent System

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The Xoft Axxent System

- Complete system for delivering breast brachytherapy
 - More indications in future
- Balloon based Accelerated Partial Breast Irradiation (APBI)
- High dose rate (HDR)
 - Complete treatment is 10 fractions in 5 days
- X-ray based rather than isotope
 - No radioactive material
 - 50 kVp versus average energy > 300 keV for Ir-192

Family Photos

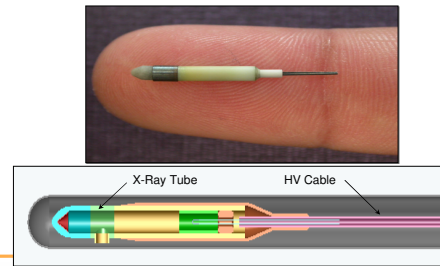


Axxent X-Ray Source

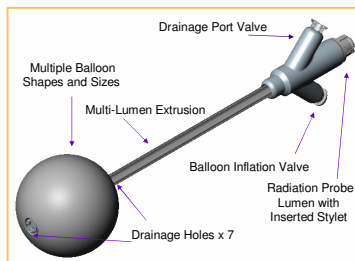
- Miniature X-ray tube for therapeutic radiation treatment
 - 2.2 mm diameter by 10 mm long
- Initial indication is breast brachytherapy
 - Over 40 patients treated since March 2007
 - Vaginal applicator under review by FDA
- Operates up to 50 kV at up to 300 μ A beam current
 - Up to 1 Gray/minute dose rate at Rx point (3 cm balloon)
 - Equivalent to a fresh Ir-192 source

X-Ray Source Design

- High vacuum end-firing x-ray tube

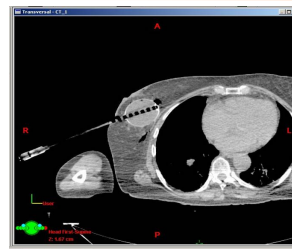


Axxent Breast Balloon Applicator



Integral Drain built into Applicator for seroma management potentially improves dosimetry and reduces infection rate.
Radiolucent Balloon Wall for improved visibility on planar film and in CT images.

Barium-Infused Balloons



CT Image taken during training.

- Good visualization of balloons under CT and Fluorographic examination. Also clearly visible using ultrasound
- Standardized contrast concentration in balloon wall material minimizes radiation attenuation

Axxent Controller

- Friendly interface to guide user thru the treatment
- Provides power and cooling to source
- Highly adjustable arm
- Built-in well chamber, electrometer for calibration
- Portable
- Safety interlocked



New X6 controller, set up for vaginal indication

From the Patient's Point of View

Implications of X-Ray Versus Radio-isotope - 1

- 50 kVp x-ray radiation is easily shielded
 - No need to treat in the vault – can use rooms with light shielding
 - Frees up vault for use with the big external beam machines
 - Staff can be in the room with the patient
 - Excellent feedback from first patients on this aspect
- Therapy is more appealing and accessible to patient population
 - Dose-depth profile of 50 kVp X-ray targets 1-2cm depth of tumor bed
 - But spares more distant critical structures
 - Allows radiation satellite centers/community hospitals to have access to HDR brachytherapy

Implications of X-Ray Versus Radio-isotope - 2

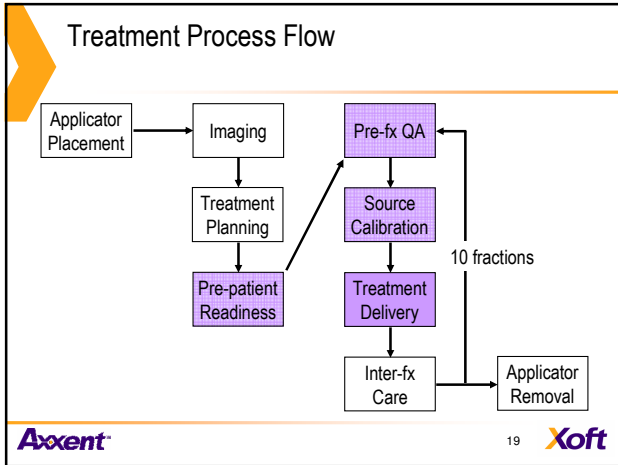
- Logistical / Regulatory
 - Licensing is much easier for X-ray than a 10 curie source
 - Think Homeland Security
 - Eliminates concerns about handling and disposal of isotope sources
 - No risk of unintended exposure
 - Source turns off when not in use
- Financial
 - Does away with high cost of radiation capital equipment infrastructure
 - Removes HDR or bunker capacity constraints currently limiting patient throughput
 - Pay as you go – disposable source rather than the fixed cost of a decaying radio-isotope

Patient Eligibility – Inclusion Criteria

- ≥ 50 years old females with good general health
- Tumor with Tis, T1, N0, M0 (AJCC Classification)
- Invasive ductal carcinoma (IDC) or ductal carcinoma in situ (DCIS)
- Negative surgical margins ≥ 1 mm in all directions prior to brachytherapy treatment
- Spacing between balloon surface and skin ≥ 7 mm
- Patient available for applicator placement within 5 weeks of lumpectomy
- Applicator is likely to fit based on lumpectomy cavity created

Treatment Planning

- BrachyVision or Plato Treatment Planning software supported
- Verify placement for Treatment Planning using CT
 - Use NSABP imaging guidelines
- Dosimetry data primarily obtained from the DVH
 - PTV should exclude the balloon volume
 - Skin dose: use isodose lines to determine point dose to skin
 - Rib dose: use isodose lines to determine point dose to rib surface



Source Characterization and Measurements

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TG43-U1 Parameterization

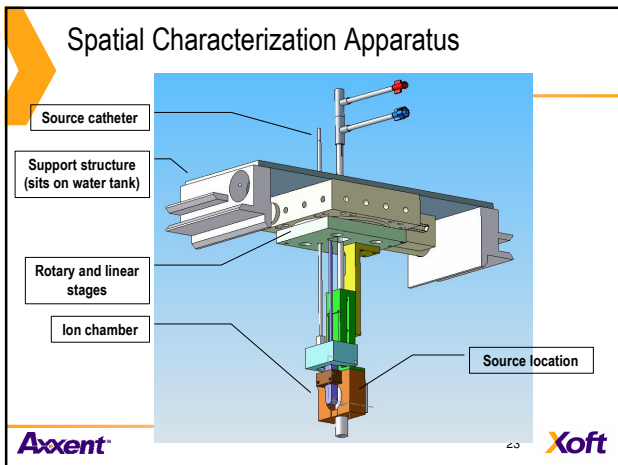
- Quantification of X-Ray output via TG-43U1 parameterization
 - Terms for Source strength, dose ratio air/water, spatial distribution
- Spatial characterization includes polar, azimuthal angle and depth-dose distributions

$$\dot{D}(r, \vartheta) = S_k \cdot A \cdot \left(\frac{r_0}{r}\right)^2 \cdot g_p(r) \cdot F(r, \vartheta)$$

Labels for the equation: Dose rate (pointing to the dot over D), Intensity terms (pointing to S_k), Geometry term (1/r²) (pointing to (r₀/r)²), Depth-dose (pointing to g_p(r)), and 2d anisotropy (pointing to F(r, ϑ)).

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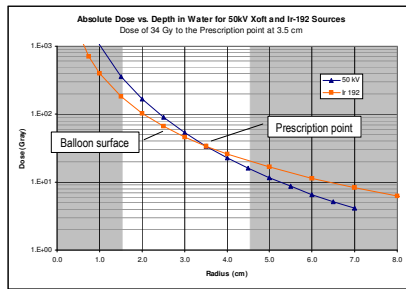
- ### Spatial Characterization Apparatus
- Custom apparatus developed to allow precision measurements of the dose distribution in 3 dimensions
 - Ionization chamber encased in solid water case, immersed in water bath
 - Detector assembly mounted to a linear stage, attached to a rotary stage, both under computer control
 - Source position controlled by manual micrometer stages in 2 dimensions, fixed in third dimension
 - Note – Monte Carlo was also extensively employed
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- ### Depth-Dose Measurements
- Depth dose (DD) measured in water phantom
 - Air ionization chamber attached to precision linear stage
 - Range from 10 to 70 mm from source center
 - Positional accuracy ~± 100 μm
 - DD characteristics dominated by point source 1/r² effects
 - Radial Dose Function (RDF) removes the 1/r²
 - Normalized to 1.0 at 10 mm from the source
 - Remainder of change is due to attenuation in the medium
 - Double exponential fit to data has residuals of ~0.5%
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Depth-Dose Compared to Ir-192

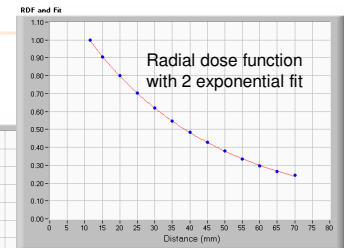
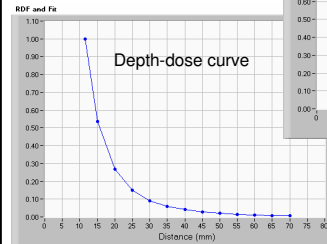
- Same dose as Iridium-192 at the prescription point
- Higher dose inside balloon applicator
- Lower dose far away (less shielding needed)



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Depth-Dose and RDF Plots



All sources are measured at 5 mm steps
Must be within 0.03 of TG43 reference to pass

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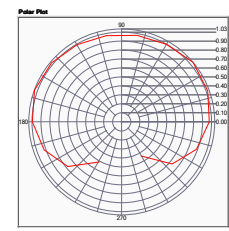
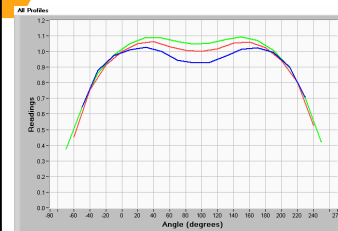
Polar Angle Distribution

- Polar distribution as a function of distance is the TG43 "2d Anisotropy Function"
 - Normalized to 1.0 at 90 degrees
 - Averaged over left/right sides in TG43
- Measured using ion chamber positioned with a rotary stage in water phantom
- Precise location of source is critical to accuracy and reproducibility

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Polar Anisotropy Data



Data at 2, 4 and 6 cm averaged over ~20 sources
Blue = 2, cm, red = 4 cm, green = 6 cm

Polar plot of averaged 4 cm results

All sources are measured at 2 orientations
Must be within 0.10 of TG43 reference to pass

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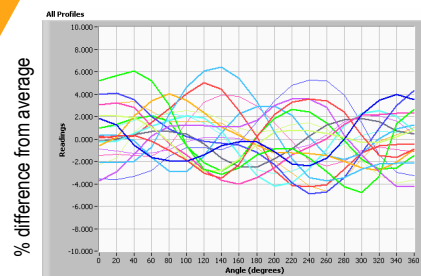
Azimuthal Angle Distribution

- Azimuthal angle goes around the source "equator"
 - Ideally would like there to be no dependence
- Measured similarly to Polar angle, but with the source entering the apparatus at right angles
- Difficult measurement due to alignment considerations
 - A "perfect" source, misaligned by just 100 μm would show a 1 – 2% effect, depending on distance
- Results plotted as "% difference from average" at each point

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Azimuthal Angle Data



Max difference < 7%,
RMS variation 2.3%

Azimuthal distributions for 20 recent sources, at 2 cm from source
All sources are measured, and must be within $\pm 7\%$ to pass

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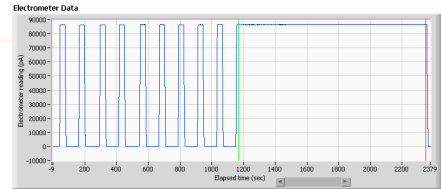
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Output Stability

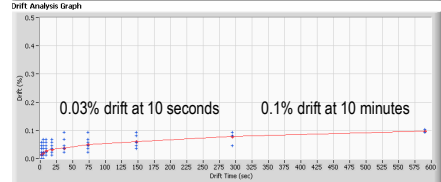
- Measurements of output strength in Air Kerma and “dose rate constant” Λ provide overall scaling factors
 - Strength similar to a new Ir-192 seed
- We look at stability of the source at short and long time scales
 - Average and maximum deviations looked at over 10 second and 5 minute scales
- “Robustness” evaluated by cycling on and off repeatedly
 - Look for consistent output each cycle
- All sources are measured before potential clinical use

Stability and Robustness Data

10 on/off cycles plus
20 min steady running



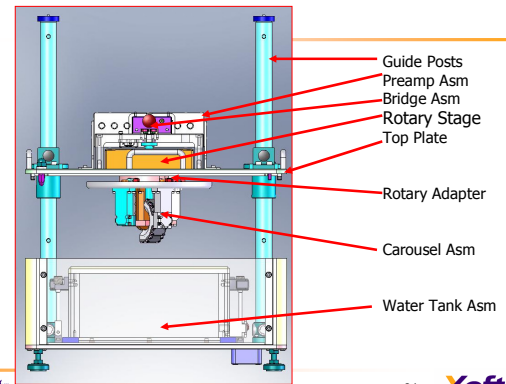
Max deviation drift
analysis using data
from steady running
segment



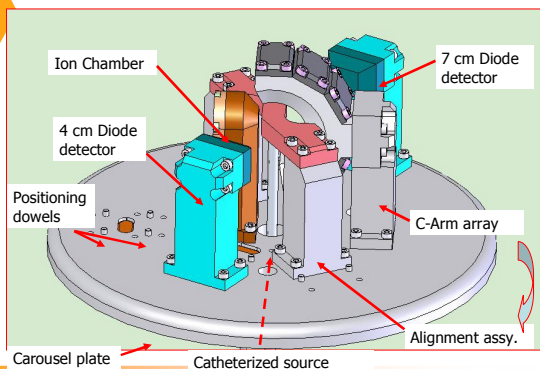
A New Manufacturing Test Fixture

- Have just completed V&V of a new fixture for routine source testing
 - Many inches of paperwork!
- Physically more robust than previous fixture
 - Tighter spatial specs
- Higher throughput, lower maintenance
- Uses 1 ion chamber, multiple scintillator/photodiode detectors
 - All cross-calibrated to the ion chamber

MTF Mechanical Design



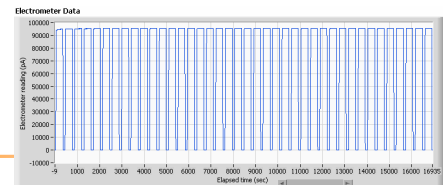
Carousel Assembly Showing Detectors



Other Source Testing

- Operational Life Testing
 - 40 5 minute cycles – see below
- Shelf life and Shipping Testing
 - 40 cycles, then redo all spatial characterization
- Clinical Simulation Testing (10 fractions plus calibrations)
 - Using Xoft system controller rather than lab hardware

40 cycle test:
5 minutes on, 30
seconds off



More Physics-y Stuff

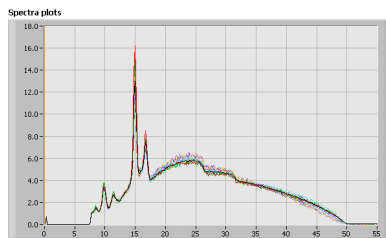
Beyond Routine Manufacturing Testing

- We're proud of all the testing we do, both routinely and as part of our Validation process
 - It's good for potential users to know how thorough we've tried to be
 - But it's kind of boring stuff
- We've also done some interesting work

X-ray Spectra Using CdTe Spectrometer

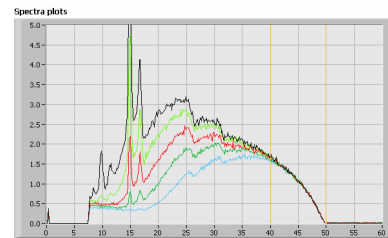
- Measured spectra of 15 sources
 - Black trace is a separate 10 Sx average
 - Bin-by-bin variability is ~5%

•This is done fairly routinely in our labs
•Spectra have also been taken at U. Wisc. and NIST using cryogenic Ge spectrometers



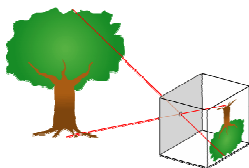
X-ray Spectra With Absorbers

- Same source, using Solid Water absorber
 - 0, 4, 10, 20 and 37 mm



Pinhole Images - Principle

- A very good way to see things upside down



▪ Key fact: The last Sunday in April is "Worldwide Pinhole Photography Day" - Wikipedia

Pinhole Images – Apparatus Description

- Source held inside a brass enclosure, with a 30 μm pinhole
 - Can look at either the end or the side of the anode
- Shadocam image plane* used to capture x-ray images
 - X-ray sensitivity 10 – 50 kV
- The x-ray launch points closely match electron distribution
 - Little scatter in the anode
- Ran sources at various kV and μA operating points
 - Typically integrated for 10 seconds

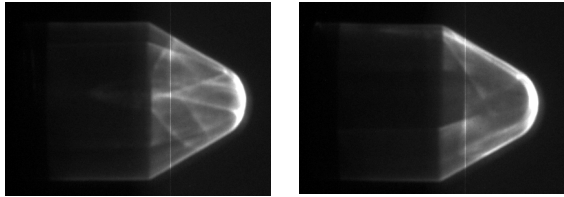
* Shad-o-Snap 1024, Rad-icon Imaging Corp

Sample Images – Side View

- Model prediction →

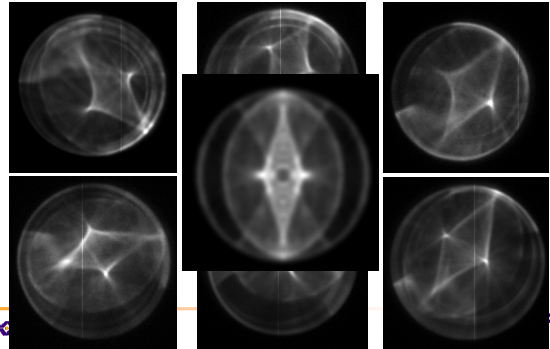


- Actual images



Sample Images – “Typical” End View

- Central diamond and surrounding oval are clearly visible

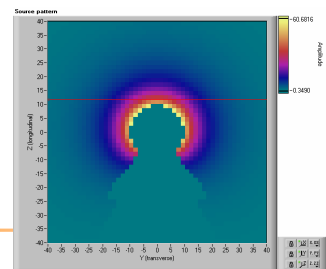


Volumetric Analysis

- Took spatial data (depth-dose, polar and azimuthal) at multiple distances, at high angular resolution
 - Combined using appropriate interpolation functions into a volumetric array
- Did same for a TG43 based data set
 - Compared individual sources to TG43 reference
- Can look at absolute dose difference, relative difference, and dose-error histograms

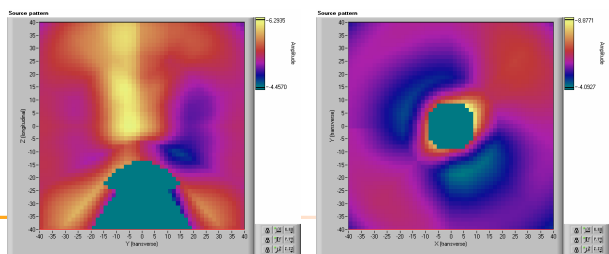
Volume Rendering of Dose Distribution

- Here is a slice through the mid-plane of the volume
- Source enters from bottom
 - Source cable prevents data acquisition in lower section



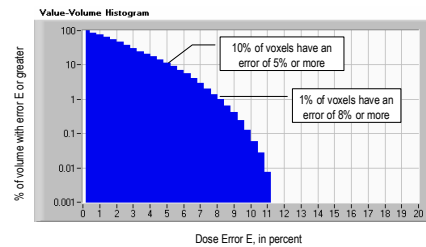
Percent Differences in Dose

- Slices near the center of a volume that is the percentage difference between an individual source and the standard
 - One slice is in the plane of the source, the other is perpendicular to it



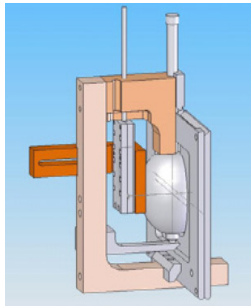
Error Volume Histogram for Source s/n 3698

- This histogram summarizes the frequency of differences (or errors) between a given source and the standard, similar to the cumulative dose histogram but with percent errors as the parameter.



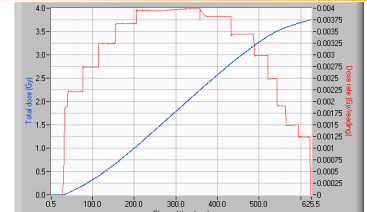
Treatment Plan Validation

- Ran simulated treatments in water phantom
- Monitored output at prescription point with ion chamber
 - Compared to plan dose
- Exposed radiochromic film
 - Compared to plan isodose contours



Dose at Prescription Point

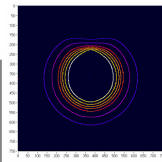
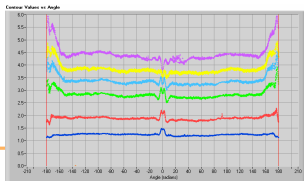
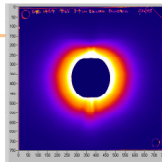
- Red trace is dose rate as source is stepped
- Blue trace is integrated dose



| X-ray Energy | Balloon Size / Shape | Rx Dose | MsrD Dose | MsrD / Prescription |
|--------------|-----------------------|---------|-----------|---------------------|
| 40 kVp | 34 mm spherical | 4.0 Gy | 4.18 Gy | 1.045 ± .08 |
| 40 kVp | 50 x 70 mm elliptical | 4.0 Gy | 4.16 Gy | 1.04 ± .05 |
| 50 kVp | 34 mm spherical | 3.4 Gy | 3.04 Gy | 0.89* |
| 50 kVp | 50 x 70 mm elliptical | 3.4 Gy | 3.45 Gy | 1.015 ± .12 |

Film and Plan Isodose Comparison

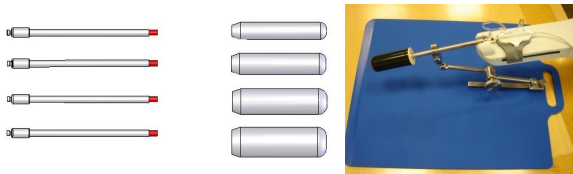
- Image processing allows quantitative evaluation
 - BrachyVision isodose lines converted to a mask
 - Overlaid with calibrated film image
 - Contours then “unwrapped” in software



Future-y Stuff

Endometrial Applicator

- Rigid cylinder applicators at radii of 2, 2.5, 3 and 3.5 cm
- Vaginal (endometrial) and rectal indications
- Currently under FDA review
- Uses same source, updated controller (FDA cleared)

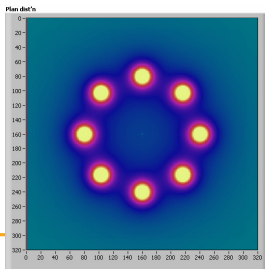


Other Future Indications

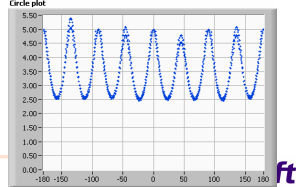
- We've heard many requests from rad oncs, physicists and even surgeons
 - Ideally we would go everywhere a seed is used
 - Will require a yet smaller source in some cases
- Intra-operative (IORT) is one area which can use the existing source
 - Takes advantage of the low shielding requirement
 - Include skin in this category

Multi-Lumen Catheters

- Simulated 8 lumen Ir-192 balloon replacement (2D)
 - Sources on 2 cm radius



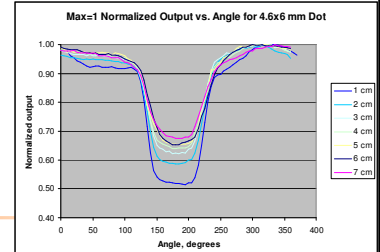
- Line plot shows dose around a circle of 2.5 cm radius
 - Max/min = 2.20



Dose Sculpting - Future Possibility

- Soft 50 kVp spectrum allows easy attenuation
 - Can create lower dose areas, say to spare close-spaced skin
- Measurement of azimuthal distribution with a "dot" placed on the source cooling catheter

- Dot is 0.001" silver foil, 6 x 4.6 mm
- Scans with ion chamber at distances from 1 to 7 cm
- Silver has "magic properties"
 - Minimizes beam hardening
 - Due to K-edge interaction with the spectrum



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Thank You!

- Xoft is now located in Sunnyvale, CA
- <http://www.Xoftinc.com>

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