Ultrasound Guided Prostate Implants
Task Group - 64
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TG-64 Report
- History
- Procedure
  - Volume Study
  - Treatment Planning
  - Seed Preparation
  - Implant
  - Final Dosimetry and Implant Evaluation
- Medical Physics Insights regarding USGPI’s

History of Prostate Implants
- Pasteau and Degrais - 1913 Radium Intra-urethral
- Radium tubes inserted through the perineum or bladder
- Flocks - 1952 Injection of Colloidal Gold-198
- Gold-198 seed implantation
- Brachytherapy treatment of the prostate died out in the 1960’s due to technical difficulties and complications as well as EBRT’s advance

I-125
- Hilaris and Whitmore MSKCC - 1972
- Retropubic approach - open procedure with direct visualization of the prostate
- 5 yr survival - 79% 606 patients
  - 96% survival T1
  - 76% survival T2
  - 69% survival T3
  - 13% survival T4

Comparison with EBRT
- Morton and Peschel - Yale University 1988
  - Retropubic Implant vs EBRT - 9 year disease free survival
    - 88% vs 74% for stage A2
    - 62% vs 63% for stage B
    - 30% vs 37% for stage C
- Schellhammer et. al.
  - Retropubic Implant - 5 year disease free survival
    - 95%, 65% and 34% for well, moderate and poorly differentiated lesions

Complications of retropubic prostate implants
- Fowler et.al.
  - Intraoperative
    - nerve injury 4%
    - excessive bleeding 2%
  - Postoperative - 23%
    - lymphoceles, hematomas, abscesses, cellulitis and wound complications
    - pulmonary embolism, - 7%
    - obstruction
Late complications - 28%
- lymphedema, voiding symptoms, rectal symptoms, impotence, wound healing, hematuria

* Retropubic approach
  - Poor seed and dose distribution
  - Significant complications
  - Poor long term clinical control
  - Walsh nerve sparing prostatectomy
  - High energy EBRT

* Nag 1985 - TRUS and Fluoroscopy guided implants
* Blasko, Grimm and Ragde
  - Seattle technique
  - Popularized prostate implantation

Advantages of the Transperineal Approach
- Avoids the morbidity of laparotomy
- Outpatient procedure
- Early recovery and return to normal patient lifestyle
- Minimal bleeding
- Low long term morbidity
- One time procedure
- Well tolerated
- Maintenance of sexual function

Procedure for Implantation
- Volume study
- Planning
- Seed preparation
- Procedure
- Final Dosimetry and Evaluation

Volume Study
- Stepwise ultrasound scans through the prostate
- Patient in same position as during implant procedure
- 1/2 cm steps
- Virtual grid on US scan
- Displacement of Prostate by US probe
- Volume determined by CT, MR and US
  - Not in agreement
  - Plexus - Neuro-vascular
- US - Gold standard for Volume determination in Urology
  - Deformation of Prostate by probe
  - Prolate ellipsoid
    - 4/3 Π a b c
    - 4.19 a b c
    - 0.52 A B C

US vs CT vs MRI Prostate
- CT - largest volume
  - 15-30% larger than US
- MRI
  - Variable, but slightly larger than US
- US
  - Used for planning
  - Margin may be used
RTOG Study Margin
- Expand US volume 2-3 mm in the anterior dimension
- Expand US volume 2-3 mm in the lateral dimensions
- Maintain posterior border
- Expand US volume 5 mm cephalad and caudad

RTOG Study
- CTV - Clinical Target Volume
  - Pre-implant TRUS prostate
- PTV - Planning Target Volume
  - Expanded CTV
- ETV - Evaluation Target Volume
  - Post implant CT definition of the prostate

Planning
- Transfer US images to TPC
  - Digitize images
    - Prostate
    - Urethra
    - Other structures
  - Capture video image in computer
    - Contour prostate and urethra on screen
  - Add appropriate margins
  - Overlay implant template
- Determine prescribed dose
  - 144 Gy I-125 Implant alone
  - 120 Gy I-125 XRT + Implant
  - 115 Gy Pd-103 Implant alone
  - 90 Gy Pd-103 XRT + Implant
- Distribute seeds in prostate using TPC tools
  - Follow one of several philosophies
- Guess initial activity and adjust seeds and activity as needed

Prostate Margins
- Margins constitute dose escalation
- Increase in seed number and seed strength
- Seeds in dissolvable suture
- Seed placement error
- Neuro-vascular bundle
- Seed migration to lung

Seed Placement Philosophies
- Uniform Loading
  - 1 cm grid
- Modified Uniform Loading
  - Eliminate seeds around the Urethra
- Non-Uniform Loading
  - Uniform loading with several central needles removed
- Peripheral Loading
  - Either high activity or 2X the number of seeds on the periphery
Implant Philosophies
■ Seed activity
■ Urethral dose
■ Rectal dose
■ Seed placement error
■ Seed migration
■ Prostate size
■ Seed Number

Implant Philosophies
■ All approaches can meet goals
  ◆ Coverage
  ◆ Urethral and rectal sparing
■ DVH analysis of preplan
  ◆ Compare different implant philosophies
  ◆ Adjust seed Air Kerma Strength to optimal
■ Automated methods of preplanning
  ◆ Yu et. al.

Rational for Modified Uniform and Peripheral Loading
■ Disease is in periphery of the prostate gland
■ Location where seed location is most critical is the periphery
■ Lower Urethral dose
■ Dosimetry
■ Patterson Parker

Source Activity
■ SmPD - Total source strength required to achieve 1 Gy in the mPD
■ Source strength calculated from nomograph or formula
  ◆ Lowell Anderson
    ◆ $I - 125 = 0.014 d^{2.05} \text{ U/Gy-mPD}$
    ◆ $Pd - 103 = 0.056 d^{2.22} \text{ U/Gy-mPD}$
  ◆ Source strength per Gy of MPD
    ◆ $I - 125 = 0.011 d^{2.2} \text{ U/Gy-MPD}$
    ◆ $Pd - 103 = 0.036 d^{2.56} \text{ U/Gy-MPD}$

Plan Evaluation
■ Root mean square deviation of the peripheral dose
■ PUN - Peripheral Uniformity Number
  ◆ 0.67
  ◆ Ratio of mPD and mean peripheral dose
■ CN - Conformation Number
  ◆ Ratio of volume of the PTV to the volume enclosed by the mPD isodose surface
  ◆ 0.72

Plan Evaluation
■ CI - Coverage Index
  ◆ Percentage of the target covered by the isodose level
  ◆ 100% in plan
  ◆ 90% in post implant dosimetry
■ Three D tools
  ◆ Visualize dose cloud and prostate
  ◆ Adjust for minimum activity to cover
    ◆ Margin
**Prostate Volume**
- Average volume implanted at UIHC - 36.5 cc
- Measured by US slice area integration
- 3 Axis estimate of volume vs integrated volume
  - Average difference 6.3%
  - Maximum difference 19%
- Maximum size for implant 50-60 cc
- Larger prostates have been implanted with difficulty

**Average Activity Implanted**
- 100 mCi of Palladium
- 1.3 - 1.4 mCi per seed
- Range of seed activity 1.10 to 1.46 mCi
- 91 Seeds on average
- Range of seed number 33-127

**Number of Needles**
- 20 Needles average
- Range 14 to 26
- Needles on 1 cm Grid for accessibility

**Isotopes**
- I-125 seeds
  - 60 day half life
  - 27-35 keV x-rays and 35.5 keV gamma ray
  - 144 Gy typically prescribed (formerly 160 Gy)
- Pd-103
  - 17 day half life
  - 20-23 keV x-rays
  - 115 Gy typically prescribed

**Seed Preparation**
- Leak testing of seeds
  - Usually done by manufacturer
  - Check containers for residual radioactivity
- Calibration of seeds
  - 10% of seeds individually
  - 10% of seeds 5 at a time
  - Batch assay
  - Cartridge assay
  - Autoradiograph

**Seed Assay**
- Measure 10% of seeds individually
- Measure seeds in bulk
- Measure seeds in cartridge
- Measure several seeds and perform autoradiograph
  - qa of loading
  - seed uniformity

**Seed Sterilization**
- Must be done in cooperation with Nursing or ID
- Container must allow steam to reach the seeds
- Seeds are NOT self sterilized due to radiation
- Seeds may be loaded under sterile conditions
- MP should become familiar with sterile technique
- Sterilization is time limited
Seed Sterilization
- Steam sterilization
- Flash sterilization
  - 270 deg F (132 deg C)
  - 27 psi
  - 4-5 min
  - 20 min drying time
- Do not steam sterilize rapid strand
- Do not steam sterilize loaded needles

Seed Sterilization
- Steam must be able to reach seeds
  - Loosened cap or access holes
  - Cotton plug in vial
  - Care taken to prevent seeds from being evacuated from containment
- Container may be double wrapped in towels
  - Allows handling and storage

Seed Loading
- Load seeds into needles as per plan
  - Plug end of needle with bone wax or rectal suppository
  - Seeds and spacers loaded as per the plan
  - Loaded needles placed in needle box which corresponds to the plan and template
  - Loading done under sterile conditions after the seeds have been sterilized

Mick Applicator
- Seeds loaded into cartridges
- Seeds delivered loaded into cartridges
  - Reusable cartridges
  - Disposable cartridges
- Seeds calibrated in cartridges
- Seeds loaded into lunch boxes and sent for sterilization

Insertion of Seeds
- Preloaded Needles
  - Seeds loaded into needles
  - End of needle plugged with bone wax
  - Spacers (dissolvable suture) placed between seeds
  - Rapid Strand
- Mick Applicator
  - Seeds placed in cartridges
  - Mick Applicator attaches to needles

Image Guidance
- Needles seen on Ultrasound Image
- US machine places a template onto the image
- The US image’s template corresponds to a physical template lying against the peritoneum
- Needles appear as bright “stars” on the US image
- The needle track is aligned at two points
  - Parallel needle tracks are obtained

OR Equipment
- Ultrasound machine
- Ultrasound probe
- Implant software
- Stepper device
- Template
- Stabilizer device
Stirrups

**Resultant Dosimetry**

- Orthogonal films
  - Accurate Inf/Sup position of seeds
  - Tedium to identify ~100 seeds
  - Three film technique
    - LAO, RAO and AP - 45 degrees apart
    - Automated seed sort routine
  - Not correlated with anatomy

- CT
  - Inf/Sup position dependent on CT slice thickness
  - Difficult to uniquely identify seeds that appear on two adjacent slices
  - Automated seed localization routines
    - Elimination of duplicate seed ID
  - Correlated with anatomy
  - DVH

**Dosimetry Evaluation**

- D100, D90, D80
  - Dose to 100%, 90% and 80% of the target volume for dosimetric evaluation

- MPD
  - Matched peripheral dose used in conjunction with ellipsoidal approximation for prostate volume

- mPD
  - Minimum peripheral dose - isodose surface that encompasses the planning target volume

- V200, V100, V90, V80
  - Fractional volume of the prostate target that recieves 200%, 100%, 90% and 80% of the prescribed mPD

- Dose volume histograms - Target
- Dose circumference histograms - Rectum & Bladder
- Dose length histograms - Urethra
- V200, V100, V90, V80, D100, D90, D80, DVH, DCH, DLH, MPD and mPD
- Affected by edema (Waterman et.al.)
  - Average swelling 50% post implant
  - Average Half-life for resolution 10 days

- Time of imaging study and seed localization
  - Affects the resultant dosimetry
  - 3 week CT

**Evaluation Tools for Prostate Implants**

- 3 Axis post plan
- Volume comparison
- Position Histogram
- Dose Volume Histogram
- Correlation to CT
- Correlation to US
- Correlation to MRI

**Radiation Safety**

- GM and/or Scintillation detector available in OR
- Accounting of all seeds and needles shall be kept
- Scan all personnel and material leaving OR
- Survey each needle after withdrawal from Patient
- Patient exposure rate measured 1 m from abdomen

**Patient Release**
NCRP 11 commentary (1995)
NRC regulations Part 35.75
State regulations
Effective dose equivalent to the general public
  ♦ < 5 mSv (<500 mrem) to the general public
  ♦ send instructions
≤3 mR/hr at 1 m
  ♦ ~0.3-0.4 mR/hr 50 cm
  ♦ NM at 1 m
Send home with instructions - Requirement
Not necessary to strain urine and return seeds after release
Keep appraised of regulatory changes
Avoid contact with pregnant women for period of time
  ♦ 4 half lives
Children restricted from lap for period of time
  ♦ 4 half lives
Sexual intercourse permitted with condom
  ♦ 2 weeks after implant
  ♦ Condom use for 4 half lives
Any seeds should not be handled directly with hands or fingers.
Use of a plastic spoon is recommended to handle seeds.
Any retrieved seed should be stored away from people in a foil wrapped container such as a glass jar.

**Equipment**
- Involvement in equipment selection
- Imaging shall be verified
  - Grid pattern and template
  - Bucket of water, grid and needles
- Fluro in OR has minimal distortion
- Acceptance test of US unit
- Applicators, accesssories, stabilizers, etc.

**Treatment Planning System**
- TG-43
  - Check planning system results versus single seed calculation
  - Check planning system with dosimetry atlas
  - Check planning system with multiple seed calculation

**Seed Assay**
- Check dosimetry system constancy using long lived isotope
- Chamber calibrated at ADCL
- Survey meter checked before use in OR
Seeds
- National Air Kerma Strength standard
- TG-43 constants
  ◆ Change from 160 to 145 Gy
- Anisotropy
- New seeds
- Changes in seed calibration
  ◆ NIST

Procedure
- Physics staff in OR during procedure
- Accounting of seeds and needles
- Surveys
- Patient release

Post Implant Dosimetry
- Quantitative analysis of implant quality
- DVH’s
- DSH
- DLH
- D90
- V200
- D100, D80, V100, V90, V80

Training
- 5 cases under supervision of experienced physicist
- Experienced physicist defined as one who has been involved in 20 or more cases
- Attend training course

Future Directions
- Anisotropy
- Interseed effect
- Tissue heterogeneity
- Biological models
- RBE
- Edema time course
- Differential dose planning and delivery

Future Directions
- Intra-operative seed localization and dosimetry
- Correlation of dosimetry and clinical outcomes
- New seed designs

Discussion
- Seed implants offer an alternative to surgery and external beam radiotherapy
- Advantages
  ◆ Outpatient procedure
  ◆ One day
  ◆ Minimum of side effects
  ◆ Extremely conformal treatment
- Can be used in combination with External Beam radiotherapy as a boost
- Concerns
  ◆ Operator dependent
  ◆ Short history in general practice
  ◆ Cost???
- Physicist plays key role in implant
  ◆ Planning, OR, Safety, Post implant dosimetry, Evaluation of implant, prediction of outcome, feedback to improve technique