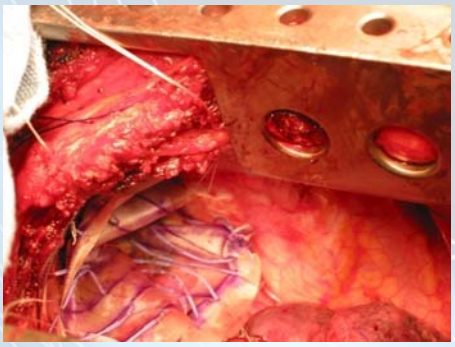
Interstitial Brachytherapy for Lung Cancer: Techniques and Results

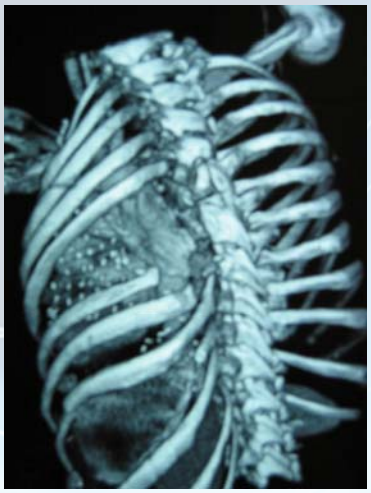
Alexandra Stewart, DM, MRCP, FRCR
University of Surrey
St Luke's Cancer Centre
Guildford, United Kingdom

Disclosures

Alexandra Stewart, DM, MRCP, FRCR, does not have any financial relationships or products or devices with any commercial interest related to the content of this activity of any amount during the past 12 months.

Interstitial Seeds





Indications

- Sublobar lung cancer resection
- Incompletely resected tumor/unresectable tumor for radical treatment
- Areas of close margin as an alternative to EBRT
- Palliative implantation of unresectable tumor for pain relief and local control

Methods of Seed Placement

- Direct placement of seeds into tumor – volume implant
- Seeds in suture sewn directly into tissue
- Seeds in suture in geometric pattern on mesh or foam grid – planar implant

Volume Implants

- Free seeds, usually I-125, dropped into a tumor using a needle, e.g., with a manual applicator, individually or in a line

MSKCC Open Volume Implant Experience

- 470 NSCLC patients from 1956–1976*
- Volume implants of tumor, positive nodes and chest wall if invaded
- 5-year local control
  - 78% stage I and II
  - 67% stage III
- 1977–1980: 88 patients T1-3 N2 M0**
  - 48/88 underwent permanent I-125 implant of residual tumor/grossly enlarged nodes
  - All 88 underwent temporary Ir-192 implant of superior mediastinum
- Locoregional control: 76%
- 2-year survival: 51%

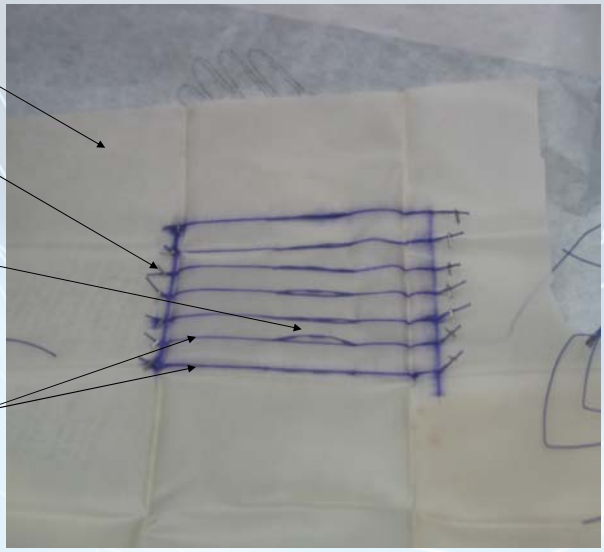
*Hilaris IJROBP 1979 **Hilaris IJROBP 1983

Percutaneous Volume Implants

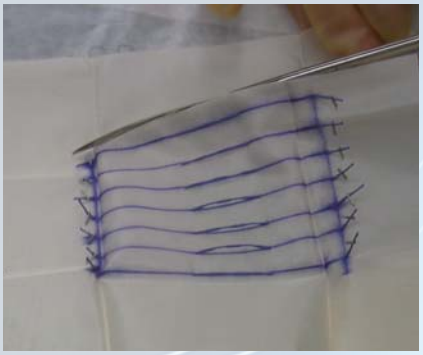
- 41 patients – 77 lesions*
- CT-guided implantation using pre-plan
- CR 64%, PR 12%, SD 13%
- At 1 year, 91% PFS, 87% OS
- 21 patients, median lesion size 4.6 cm**
- CT-guided implantation using pre-plan
- CR 29%, PR 43%, SD 14%
- At 1 year, OS 42%

*Huang et al 2013, **Wang et al 2011

Planar Implants

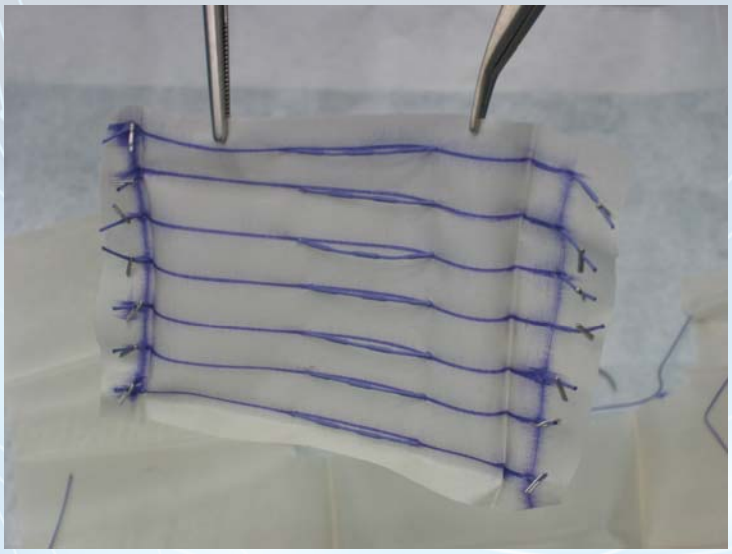


Completed implant is cut to size using long-handled scissors, allowing adequate margin for surgeon to suture

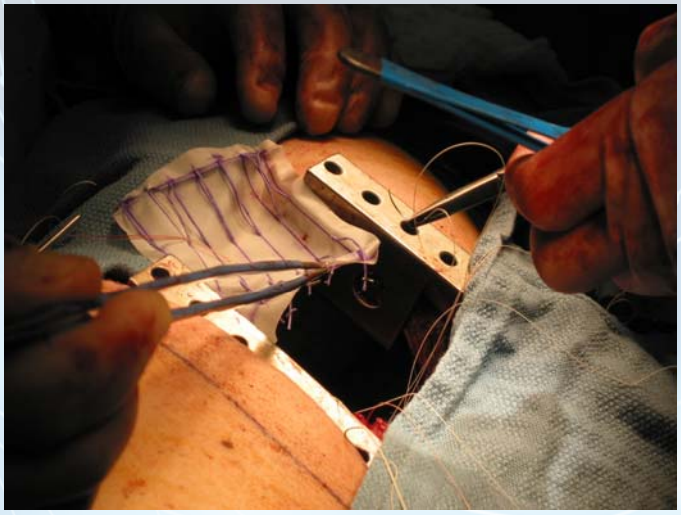


Seeds in suture are stored in sterile steel rings that are surveyed prior to discarding at the end of the procedure

Completed implant is handled only with forceps



Implant being stitched into place using long-handled tools -
Care is taken not to stitch through a seed!



Sublobar Lung Resection

- Allegheny General Hospital, Pittsburgh-retrospective case-matched series
  - 101 Stage I NSCLC patients undergoing sublobar resection (SR) and intraoperative brachytherapy (Jan '97-July '02)
  - Compared to 102 stage I NSCLC patients undergoing SR alone (Jan '89-July '94)
  - All patients had SR due to poor cardiopulmonary reserve
- Prescribed dose 100–120 Gy at 0.5 ~~mm~~ cm
- Procedure added approximately 15 minutes to anesthesia time

Santos et al Surgery Oct 2003 691-7

Results

	Brachytherapy	No Brachytherapy
Median follow-up in months	18 (range, 1–62)	24–29
Local recurrence rate	2% (P = 0.0001)	18.6%
Regional/distant recurrence rate	28.4%	23%
2-year survival	73%	70%

ACOSOG Z4032

Patients with one major criterion or two minor criteria:

Major

- FEV_1 <50% predicted
- DL_{CO} <50% predicted

Minor

- Age ≥75 years
- FEV_1 51–60% predicted
- DL_{CO} 51–60% predicted
- Pulmonary hypertension (PA systolic pressure >40 mm Hg)
- LVEF ≤40%
- Resting arterial pO2 ≤55 mm Hg or SpO2 ≤88%
- pCO2 >45 mm Hg
- MMRC dyspnea scale ≥3

ACOSOG Abstract Results

- Randomized to sublobar resection +/- brachytherapy along suture line
- No difference between the groups
- Full results awaited
- Not recommended outside clinical trials

Paraspinal Brachytherapy

- 2 retrospective series including thoracic spine implants
- Planar and volume implants
- Average cumulative cord dose 60–70 Gy
- Local control 51–84%
- 2-year OS 12–24%
- No radiation myelitis despite high cord doses

Rogers IJROBP 2002
Armstrong IJROBP 1991

Paraspinal Brachytherapy

- Surgery and fractionated EBRT remains the radiotherapy treatment of choice
- Brachytherapy may be useful in previously irradiated patients or as initial management in patients with high performance status and limited disease burden

BWH Planar Implant Experience

- 59 patients with 64 implants
- Mean age 53 years (range, 15–80)
- Histology: NSCLC 44%, sarcoma 32%, mesothelioma 10%, carcinoid tumor 5%, thymic carcinoma 5%, thymoma 2%, and non-seminomatous germ cell tumor 2%
- Areas implanted: mediastinum 40%, chest wall 29%, superior sulcus 14%, vertebral body 10%, apex 5%, diaphragmatic crus 2%, and lung parenchyma 2%

Results

- Median implant area: 40 cm^2
- Median number of seeds per implant: 40
- Median implant activity: 146mCi (median activity/cm^2 0.42 mCi)
- 31 patients had prior EBRT dose range 40–68.4 Gy
- Median follow-up: 17 months (range, 0–88)
- 1 year overall survival: 94%
- 1 year local control: 80%

Major Toxicity

- G 3-4 toxicity ~11% at 12 months
  - Esophageal/bronchial fistula (3)*
  - Radiation pneumonitis (1)
  - Hydropneumothorax (1)
  - Persistent pneumothorax (1)
  - ?Aortic rupture (1)
- None after 1 year

*Stewart et al, Brachytherapy 2006

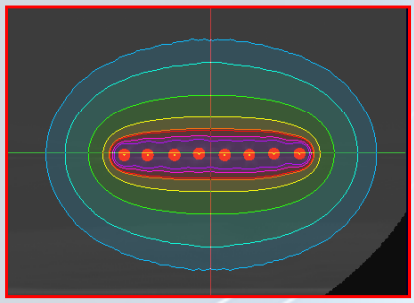
- MSKCC has used seed implants with post-operative chemotherapy within a randomized trial of chemotherapy and shown no increase in toxicity in the brachytherapy patients

Isotope Selection

Isotope	Half-life (days)	Energy (keV)	Half Value Layer (mm of lead)
Iodine ^{125}I	60.2	28	0.025
Palladium ^{103}Pd	17.0	21	0.004
Caesium ^{131}Cs	9.7	29	Minimal

Iodine-125 Seeds

- Free seeds or seeds in suture
- 5-mm seeds
- In suture: 10 seeds/strand, 1-cm spacing
- 0.5 mCi seeds ≥100 Gy vLDR at 5–7 mm



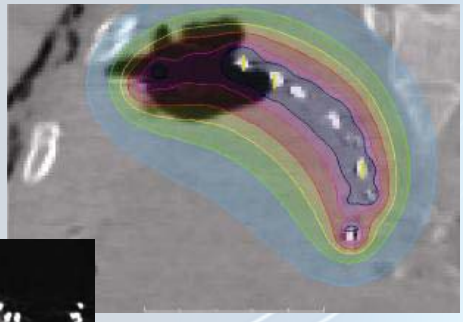
Other Isotopes

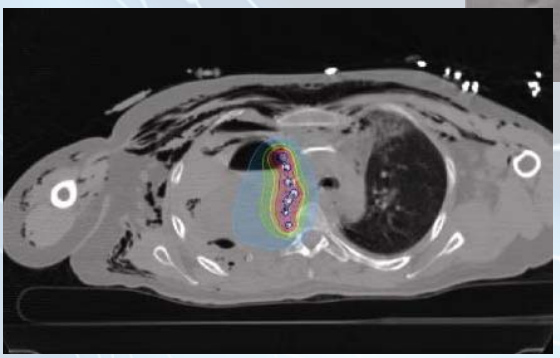
- Alternative seeds with shorter half-life may be more suited to high α/β ratio of lung cancer
- Palladium 103
  - Promising early results; difficult to obtain so not used much
- Caesium 131
  - Other properties similar to iodine 125
  - Similar dose prescriptions to iodine 125
  - Early studies indicate clinical effectiveness

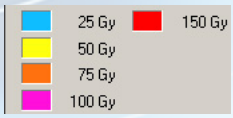
Dosimetry

- Pre-operative CT imaging and treatment planning may be used, particularly for volume implants
- Post-operative dosimetry should be performed for quality assurance and dose estimation
- Usually performed using CT scanning prior to patient discharge
- Conventional prostate seed localization and dosimetry packages can be modified for use in other parts of the body

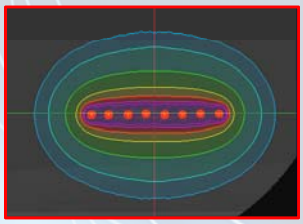
Axial and coronal isodose distributions for planar implant to right upper mediastinal target

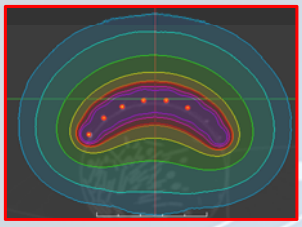






Effect of Curvature





- Isodoses on the concave side of a curvature are further from the implant surface
- Asymmetry increases with decreasing radii of curvature

Cormack et al, IJROBP 2008

Radioprotection

- Radiation survey
  - Surface of implant, 0.5 m and 1 m from implant
- Measured exposure rates at anterior skin following I-125 or Pd103 prostate implant*
  - Require 20 hours at ant skin surface and >500 hours at lat skin surface to exceed lifetime dose
- Spouse, children, pets, and rooms monitored following I-125 and Pd-103 prostate implants**
  - Calculated lifetime exposure did not exceed annual limit
  - 94% of room dosimetry did not detect radiation
- But prostate implants deeper and less accessible than many thorax implants

*Smathers 1999 **Michalski 2003

Updated ABS Consensus Guidelines

New Recommendations

- Interstitial seed treatment following sublobar lung resection recommended generally within the confines of clinical trials
- Post-operative CT planning should be performed for interstitial implants with reporting of dose to organs at risk

Stewart et al, in press 2013

Conclusions

- Seed implants can be used in highly selected patients with positive or close margins
- Care must be taken where structures acting as natural spacers have been disrupted by surgery or disease
- Outcomes may be better than those expected with surgery alone, but more clinical trials are needed