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## BACKGROUND:

Achieving durable local control for larger brain metastases remains problematic. Resection (R) alone is typically insufficient. Even with the addition of stereotactic radiation the 12-month recurrence rate for larger lesions (i.e., >2.5-3cm) is 20% or more in many series. To improve outcomes we designed and prospectively evaluated a permanently implanted radiation device consisting of Cs-131 seeds positioned within a collagen tile (GammaTile, GT Medical Technologies, Tempe AZ USA). We combined maximum safe resection and collagen tile brachytherapy (CTBT) with the hypothesis that immediate radiation initiation and/or dose intensification could improve outcomes.

## MATERIALS/METHODS:

From 2/2013-2/2018 patients undergoing resection with either previously untreated or recurrent brain metastasis were enrolled on a single arm, multi-histology study (ClinicalTrials.gov, NCT#03088579). At resection completion the tumor bed was lined with collagen tiles imbedded with Cs-131, delivering 60-80 Gy at 5 mm depth. The device was designed to prevent direct source-to-brain contact and to maintain inter-source spacing after closure. No additional local therapy was given unless progression occurred.

## PREPARED COLLAGEN TILE:



2.5 x 2.5 x .4 cm collagen tile containing imbedded Cs-131 seeds at 1 cm intervals. (A) Tile shown trans-illuminated. (B), (C) are end views of the tile depicting the asymmetric source offset relative to sides of the tile. (Vicryl seen as blue threads at ends of tile; seeds are not directly visible)

## KEY INCLUSION/EXCLUSION CRITERIA:

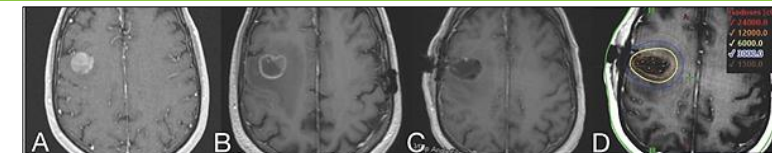
Surgically resectable but resection alone insufficient for long term control. Age  $\geq$  18. Life Expectancy > 26 weeks. KPS > 70. Total prior same-site radiation dose not to exceed 100 Gy

## PATIENT/TUMOR CHARACTERISTICS:

Age at initial diagnosis, years	58 (41-75)
Age at resection with Cs-131 tile implantation, years	60 (41-80)
Lesion location	
Parietal	7/16 (44%)
Frontal	4/16 (25%)
Temporal	3/16 (19%)
Posterior fossa	2/16 (12%)
Treatment status at time of implant	
No prior local treatment	4/16 (25%)
Prior local treatment	12/16 (75%)
If prior local treatment, types	
Resections	1.5 (0-3)
Radiation courses	1.5 (1-2)
Time to progression after prior treatment, months	4.8 (1.9-22)
Preoperative maximum tumor diameter, cm	3.1 (1.9-5.1)
Extent of resection at Cs-131 tile placement	
Gross-total	16/16 (100%)
Histology	
Breast	47/16 (44%)
Non small cell lung cancer	5/16 (31%)
Sarcoma	3/16 (19%)
Small cell lung cancer	1/16 (6%)
Karnofsky Performance Status	70 (70-90)
Cs-131 seeds implanted, No.	18.5 (5-63)
Radioactivity implanted, mCi.	71.3 (18.5-227.4)
Median observation period, months	9.3 (1.4-28)
Median radiographic follow-up, months	9.5 (<1-25.2)

Abbreviations: cm, centimeter; Cs-131, cesium 131; mCi, milliCurie  
\*All values except sex and age are given on a per-case (vs. per-patient) basis.  
Continuous variables are given as median (range). Proportions are given as fractions (percentage).

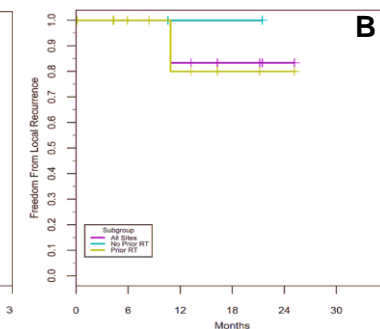
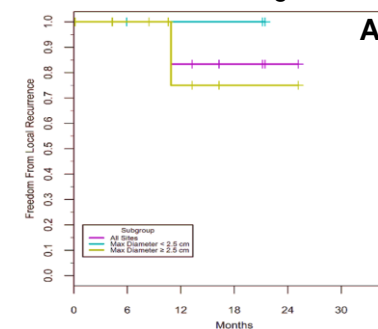
## EXAMPLE CASE:



A) MRI at initial SRS treatment; (B) MRI at recurrence; (C) initial postoperative (trial) scan with devices implanted; (D) postimplant device dosimetry with selected isodose lines; doses are in Gy. All scans are axial T1 post contrast.

## RESULTS:

N=16 metastases in 11 patient were treated; 12 tumors were recurrent and 4 were previously untreated. Median maximum diameter 3.1 cm, range 1.9-5.1 cm. Histology was 7 breast, 6 lung, and 3 sarcoma. Median age 60 years (range 41-80); KPS 70 (range 70-90); 7 females/4 males. Average time for implantation was 5 minutes. At a median radiographic follow-up of 9.5 months treatment site progression occurred in 1/16 (6%) at 10.9 months and the median treatment site time-to-progression (TTP) has not been reached (95% CI, >10.9 months). At 12 months, LC after R+CTBT for all tumors, tumors <25 mm, and tumors >25 mm was 83%, 100%, and 75% respectively. For previously untreated tumors LC at 12 months was 100% and for recurrent tumors was 80%, respectively. Median overall survival 9.3 months. Two tumor beds (12.5%) experienced radiation brain changes, one grade 2 and one grade 3 and resolved with medications. No surgical adverse events occurred.



LC by (A) maximum preoperative enhancing diameter. LC for all tumors, tumors <2.5 cm, and tumors >2.5 cm are shown. (B) LC by radiation treatment status; RT: radiation therapy.

## CONCLUSIONS:

Resection + collagen tile brachytherapy demonstrated excellent safety and local control outcomes in this single-arm pre-commercial study. The device recently received FDA clearance for use in newly diagnosed and recurrent brain metastasis. Randomized clinical trials vs standard of care treatments are expected to open in 2020.