A New Radiation Concept, Treatment of Squamous Cell Carcinoma by Alpha-radiation Based Brachytherapy (Alpha DaRT)

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ABSTRACT

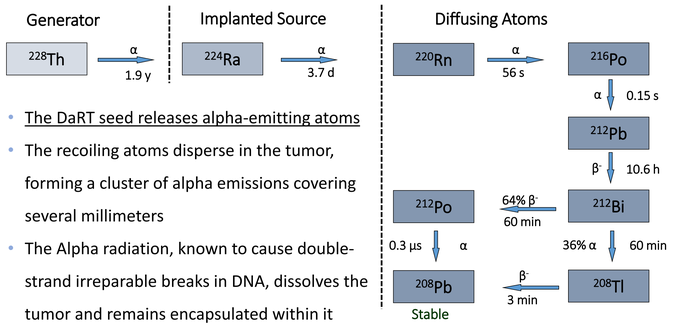
Purpose/Objective(s): The first clinical trial in humans with skin and oral cavity squamous cell carcinoma (SCC) was performed in order to evaluate the effect of a unique intratumoral alpha radiation based tumor ablation treatment termed Diffusing Alpha emitters Radiation Therapy (DaRT).

Materials/Methods: Radium-224 loaded sources (DaRT seeds) were inserted into solid tumors and released by recoil short-lived alpha-emitting atoms (Rn-220, Po-216, Pb-212, Bi-212, Po-212, Tl-208). These atoms disperse in the tumor, and spray it with highly destructive alpha radiation. The decay products diffuse in the tumor mass to a distance of at least 5 mm.

Results: A feasibility and safety clinical study is ongoing and currently 17 patients were treated at the Rabin Medical Center (Israel). Patients with histopathological confirmed skin or head and neck SCC, and tumor size ≤ 5 centimeters in the longest diameter, were enrolled. Treatment was delivered based on a CT-simulation pre-treatment plan. The seeds (1 cm long and 0.7 mm in diameter) each carrying a dose of 2 µCi were placed 5-6 millimeters from each other. CT was used to check the position of the radioactive seeds. Two to four weeks after implantation the seeds were removed, and six weeks after treatment CT was performed to assess the effect of treatment. Study results are available for 15 subjects who reached the 30-day visit. The age of the patients ranged between 66 to 94 (median 81). Six patients had oral cavity SCC and nine diagnosed with aggressive skin SCC. Eleven patients were treated within radiation failure fields (Radiation dosage >60 Gy). All tumors responded to the treatment; Eleven tumors had a complete response and four tumors showed a partial response. No major toxicity was noted.

Conclusion: In this feasibility and safety human study we demonstrated that alpha particles based DaRT exhibit enhanced radiobiological potential. The treatment was effective against radio-resistant SCC tumors without major toxicity.

INTRODUCTION



- <u>The DaRT seed releases alpha-emitting atoms</u>
- The recoiling atoms disperse in the tumor, forming a cluster of alpha emissions covering several millimeters
- The Alpha radiation, known to cause double-strand irreparable breaks in DNA, dissolves the tumor and remains encapsulated within it

CLINICAL STUDY RESULTS

KEY ELIGIBILITY CRITERIA

Inclusion Criteria

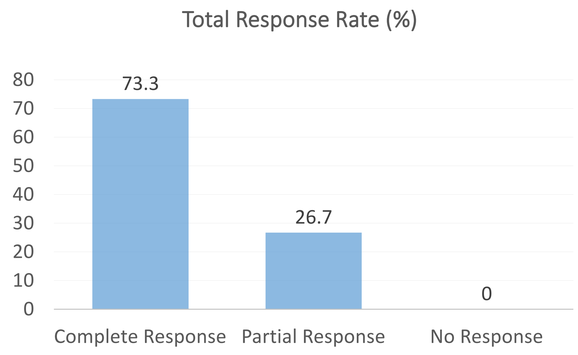
- Histopathological confirmation of SCC
- Lesions ≤ 5 cm in the longest diameter (without nodal spread)
- Age ≥ 18
- WOCBP will have evidence of negative pregnancy test
- Life expectancy ≥ 6 months
- ECOG ≥ 2

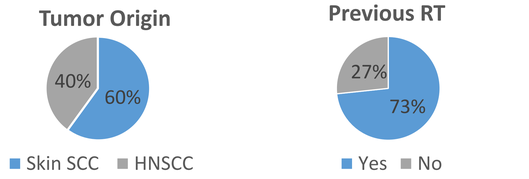
Exclusion Criteria

- Ulcerative lesion
- Tumor of Keratoacanthoma histology
- Patients with moribund diseases, autoimmune diseases or vasculitis.
- Patients under immunosuppressive and/or corticosteroid treatment.
- Participation in other studies in the past 30 days

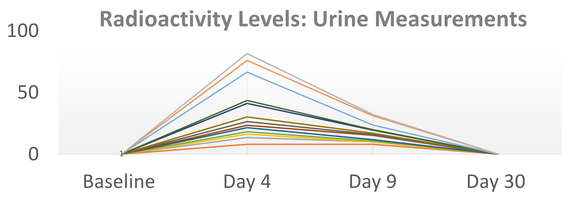
EFFICACY

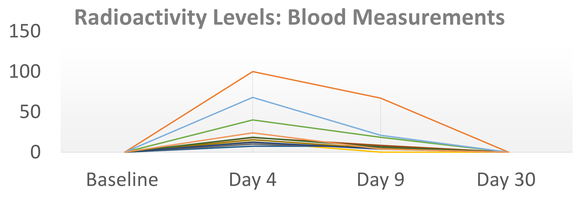
Patient	Age	Tumor Location	Previous RT	Response
AT-01	87	Mandible	Yes	Partial
AT-02	80	Ear	Yes	Complete
AT-03	94	Tongue	Yes (x2)	Complete
AT-05	75	Parotid	Yes	Partial
AT-07	94	Tongue	Yes	Complete
AT-08	69	Nose	Yes	Complete
AT-11	81	Ear	Yes	Complete
AT-12	91	Tongue	Yes	Complete
AT-13	76	Cheek	No	Complete
AT-14	78	Lip	Yes	Complete
AT-15	70	Forehead	No	Partial
AT-16	66	Lip	No	Complete
AT-17	88	Parotid	Yes	Partial
AT-18	82	Scalp	No	Complete
AT-21	81	Scalp	Yes	Complete





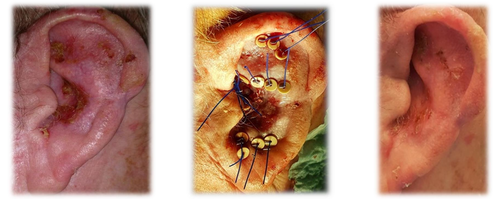
SAFETY





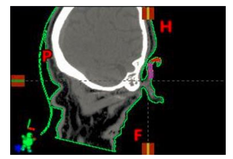
PATIENT EXAMPLE

AT 002 – Procedure date: March 21st, 2017



March 7th, 2017 | March 21st, 2017 | June 1st, 2017

Initial tumor volume (cm^3)	1.4
Alpha DaRT seeds inserted	10
Total	20
Tumor reduction	100%



CONCLUSIONS

Treatment plan

- The ideal planning should include radiotherapist, surgeon and physicist
- The planning should be based on both direct visualization and imaging
- Better understanding of the required dose and radiation distribution will improve outcomes in large tumors
- Low Toxicity, better over cover than under!

The Procedure

- The procedure is feasible, simple and can be done in relatively short time

The Alpha DaRT Treatment

- The treatment has very low toxicity and overall seems to be safe
- The treatment was proven to have the ability to destroy SCC tumors
- Complete Response over 70%!

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