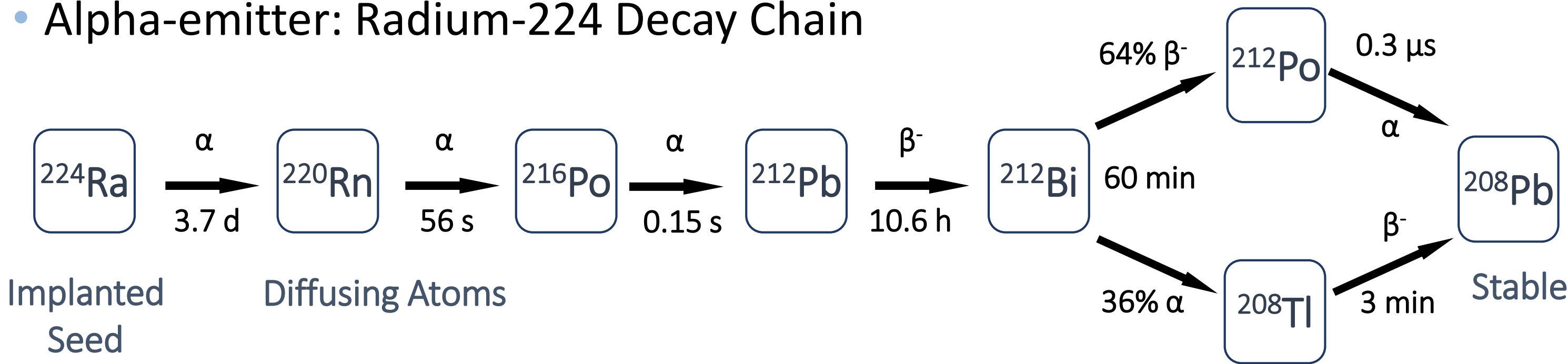


A New Alpha Particle Treatment for Recurrent or Aggressive Head and Neck Squamous Cell Carcinoma

A. Popovtzer^{1,2}, E. Rosenfeld³, R. Ben-Hur³, A. Mizrachi⁴, I. Kelson⁵, and Y. Keisari⁵; ¹Rabin Medical Center Petah Tiqva, Petah Tiqva, Israel, ²Tel Aviv University, Tel Aviv, Israel, ³Rabin Medical Center, Petah Tiqva, Israel, ⁴Rabin Medical Center, Tel Aviv, Israel, ⁵Tel Aviv University, Tel Aviv, Israel

Introduction

- The DaRT seed releases alpha-emitting atoms
- 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
- Alpha-emitter: Radium-224 Decay Chain



Objectives

The first clinical trial in humans with skin and head and neck 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).

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 approximately 3 millimeters radius around the seed.

Results

A feasibility and safety clinical study is ongoing and currently 27 cases were treated at the Rabin Medical Center (Israel) and IRST (Italy). 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 up to 5 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 18 cases who were treated per protocol and reached the 30-day visit. The age of the patients ranged between 60 to 102 (median 80). Nine patients had head and neck SCC and eighteen subjects were diagnosed with aggressive skin SCC. Thirteen subjects were treated within radiation failure fields (Radiation dosage >60 Gy). All tumors responded to the treatment; Thirteen tumors had a complete response and five tumors showed a partial response. No major toxicity was noted.

Conclusion

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

Clinical Study Results

Key Eligibility Criteria

Inclusion Criteria

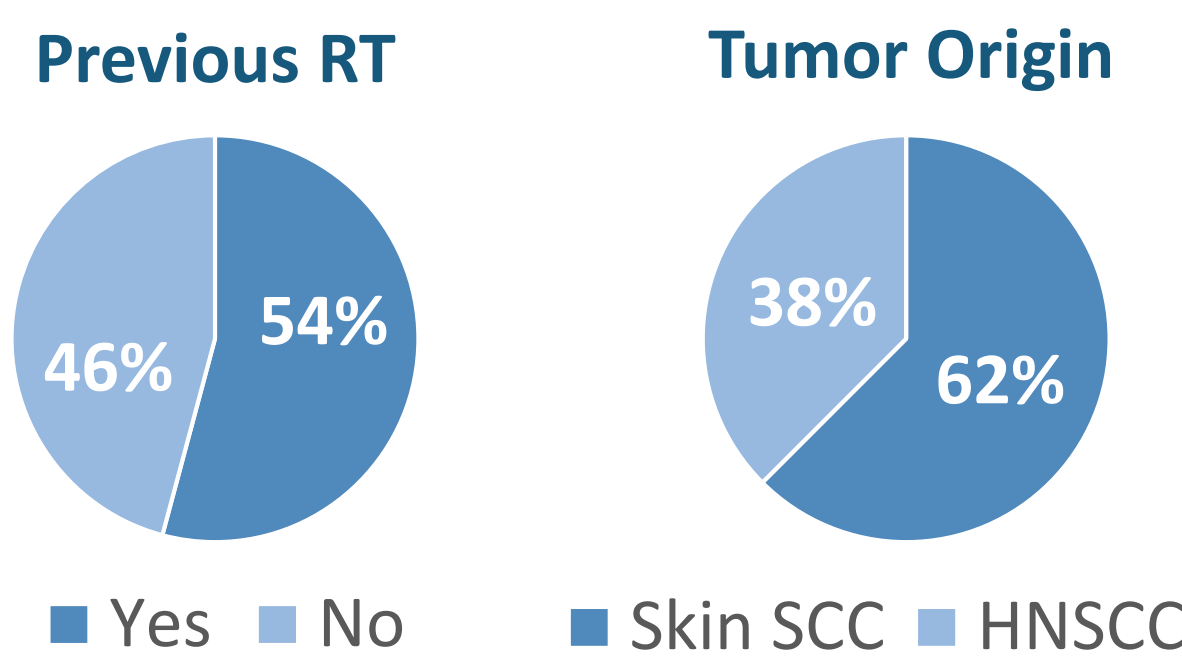
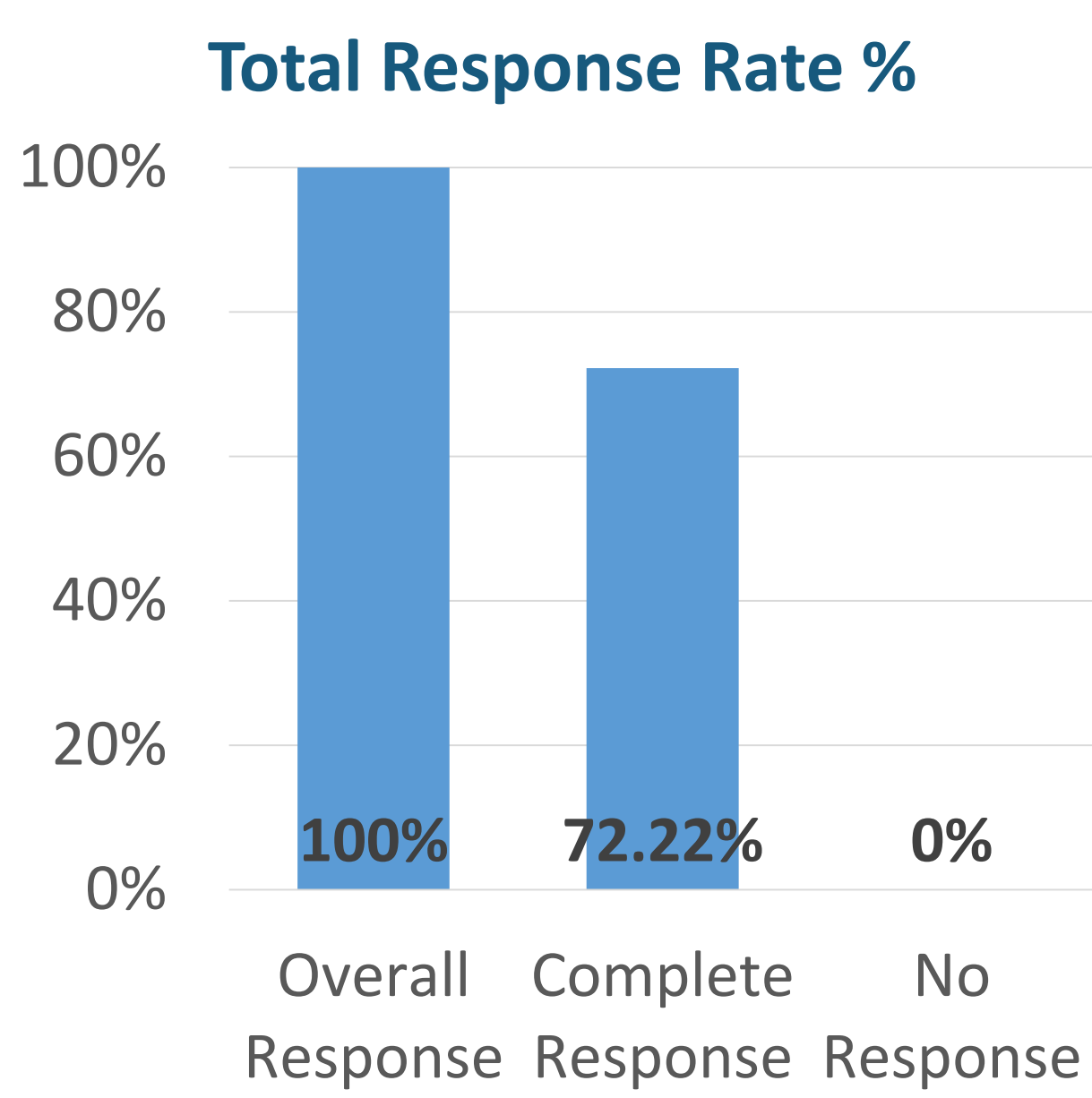
- Histopathological confirmation of SCC
- Lesions ≤ 5 cm in the longest diameter (without nodal spread)
- Age ≥ 18
- WOCBP will have evidence of negative pregnancy test
- Life expectancy ≥ 6 months
- ECOG ≥ 2

Exclusion Criteria

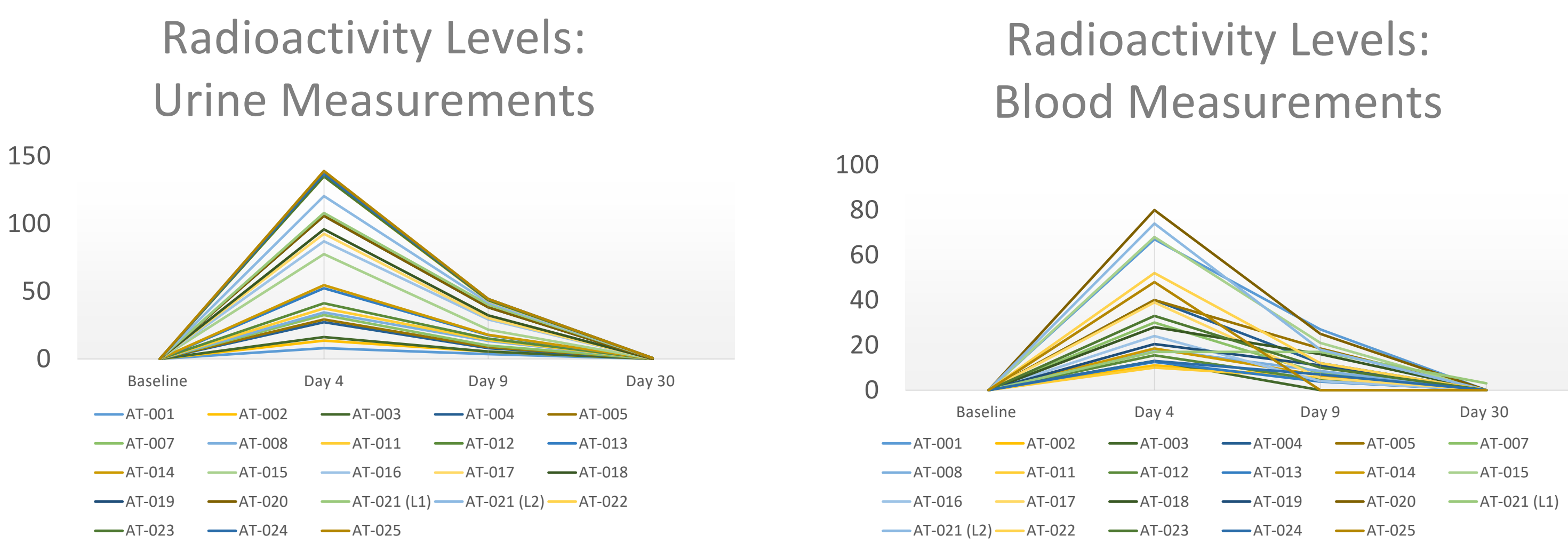
- Ulcerative lesion
- Tumor of Keratoacanthoma histology
- Patients with moribund diseases, autoimmune diseases or vasculitis.
- Patients under immunosuppressive and/or corticosteroid treatment.
- Participation in other studies in the past 30 days

Efficacy

Patient	Tumor Location	Previous RT	Response
AT-01	Mandible	Yes	Partial
AT-02	Ear	Yes	Complete
AT-03	Tongue	Yes (x2)	Complete
AT-05	Parotid	Yes	Partial
AT-07	Tongue	Yes	Complete
AT-08	Nose	Yes	Complete
AT-11	Ear	Yes	Complete
AT-12	Tongue	Yes	Complete
AT-13	Cheek	No	Complete
AT-14	Lip	Yes	Complete
AT-15	Forehead	No	Partial
AT-16	Lip	No	Complete
AT-17	Parotid	Yes	Partial
AT-18	Scalp	No	Complete
AT-21 (L1)	Scalp	Yes	Complete
AT-21 (L2)	Scalp	Yes	Partial
AT-22	Scalp	No	Complete
AT-23	Upper Lip	Yes	Partial
IRST-01	Right Calf	No	Complete



Safety



Patient Example

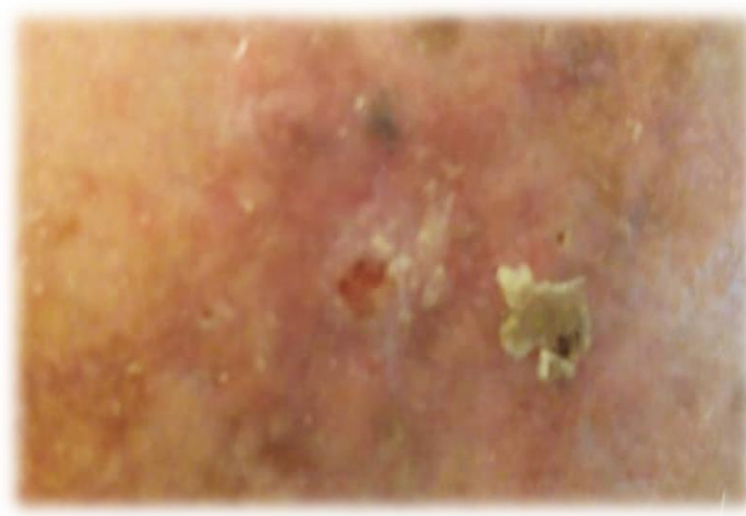
AT 22 – Procedure date: August 30th, 2018



Screening
27/08/2018



DaRT Insertion
30/08/2018



Day 30
30/09/2018

Initial tumor volume (cm ³)	2.82
Alpha DaRT seeds inserted	24
Total activity kBq	2,100
Response	100%

