Development of a 3D-printed Geiger-Müller calibration geometry to verify the activity of a novel endoscopic alpha-emitters brachytherapy (EUS-DaRT) loading device for pancreatic cancer

Y. Kamio[1,2,3], J.-F. Carrier[1,2,3] and S. Bedwani[1,2,3]

1. Centre hospitalier de l'Université de Montréal (CHUM hospital), Montréal, Canada
2. CHUM Research Center, Montréal, Canada
3. Université de Montréal, Montréal, Canada

JULY 12–16 2020 VIRTUAL
Improving Health QUALITY. Increasing Global IMPACT
JOINT AAPM | COMP MEETING
EASTERN TIME [GMT-4]

INTRODUCTION

Pancreatic cancer is associated with a poor prognosis, yielding a 5-years survival probability of 9% when all stages are combined [1]. Interstitial implantation of I-125 seeds using endoscopic ultrasonography (EUS-BT) is known to be safe with moderate clinical benefits for advanced pancreatic cancer [2,3]. Diffusing alpha-emitters radiation therapy (DaRT) has recently been shown to be safe and effective for locally advanced recurrent squamous cell carcinoma of the skin and head & neck [4,5]. **A feasibility and safety study investigating the use of diffusing alpha-emitters endoscopic brachytherapy (EUS-DaRT) for unresectable pancreatic cancer is under preparation at CHUM hospital (Montreal, Canada).**

AIM

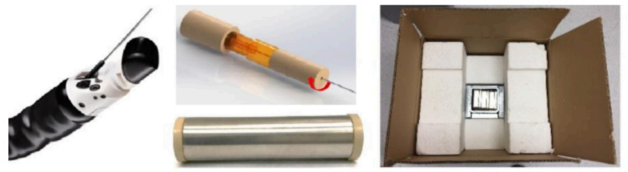

Figure 1: *[Left] EUS-guided fine needle (courtesy of Boston Scientific). [Middle] Loading device & capsule. [Right] Metal boxes and steel shielding (for shipping).*

A novel device shown in figure (1) has been developed by Alpha Tau Medical Ltd. (Tel Aviv, Israel) to safely load permanent Ra-224 seeds (Activity: 3-6 µCi, length: 1-2 cm) into an endoscopic EUS-needle for DaRT brachytherapy. **This study aims to compare three easily replicable Geiger-Müller detector calibration setups to verify the total activity of the device before use.**

METHODS

Figure 2: *Calibration geometries. [Left] Using 2 metal boxes and 5 mm steel Absorber from the shipping package (detector-to-device distance = 4 cm). [Middle] Improvement of the setup using a 3D-printed support. [Right] 3D-printed support without absorber (detector-to-device distance = 4 cm).*

The three calibration geometries (4 cm separation with/without a 5 mm steel absorber and/or a 3D-printed support) shown in figure (2) have been used to **determine γ dose-rate to Ra-224 activity calibration factors for a portable GM counter (Model: RAM GENE 1 Mark II from Rotem Industries Ltd).** Calibration measurements (n = 10) using 1 & 2 cm loading devices were performed with the daughter products in secular equilibrium. The loading devices were removed and placed back between each measurement with a 20s delay to stabilize the reading.

RESULTS

Seed length [cm]	α-spectrometry [kBq]	Calibration Geometry	Dose-rate [µSv/h] (n = 10)	Calibration factor [kBq · h/ µSv]
1	151.2	Absorber-only	11.7 ± 1.2	13.0 ± 1.3
		Absorber & 3D-printed support	13.0 ± 0.4	11.7 ± 0.3
		In-air & 3D-printed support	17.2 ± 0.4	8.8 ± 0.2
2	350.8	Absorber-only	30.2 ± 1.9	11.6 ± 0.7
		Absorber & 3D-printed support	32.9 ± 0.5	10.7 ± 0.2
		In-air & 3D-printed support	45.1 ± 0.9	7.8 ± 0.2

Table 1: Determination of calibration factors to convert γ dose-rate to Ra-224 activity for three different calibration geometries and two seed types. The uncertainties stated consider the full reproducibility of the setup (n = 10).

Table (1) shows the average value of 10 measurements performed with the Rotem GM counter in the dose-rate mode [µSv/h] for the three calibration geometries considered in this study. The γ-emission was measured with the loading devices inside their protective stainless-steel capsules and sterilization pouches. Calibration factors were then obtained by taking the quotient of the seed's Ra-224 α-activity from the manufacturer's calibration certificate and the averaged measured γ dose-rates. Ra-224 activities (151.2 & 350.8 kBq for the 1 & 2 cm seeds respectively) were determined by Alpha Tau Medical ltd. using silicon charged-particle detector α-spectrometry measurements with an uncertainty of 0.1 kBq (k = 2). The calibration factors of the 1 cm & 2 cm loading device were found to be 13.0 ± 1.3 & 11.6 ± 0.7, 11.7 ± 0.3 & 10.7 ± 0.2 and 8.8 ± 0.2 & 7.8 ± 0.2 kBq·h/µSv for the absorber-only, absorber & 3D-printed support and 3D-printed-support-only geometries.

Seed length [cm]	Calibration Geometry	Measured activity [kBq] (n = 3)	α-spectrometry [kBq]	Relative error [%]
1	Absorber-only	167.4 ± 18.3	147.5	13.5
	Absorber & 3D-printed support	147.9 ± 5.4		0.3
	In-air & 3D-printed support	148.0 ± 4.5		0.3
2	Absorber-only	353.8 ± 31.4	350.1	1.1
	Absorber & 3D-printed support	348.4 ± 10.2		-0.5
	In-air & 3D-printed support	379.1 ± 12.0		8.3

Table 2: Accuracy test using two seeds different from the ones used for the calibration. The relative error shows the discrepancies between the measured activity and the manufacturer's α-spectrometry reference

Table (2) shows the results of an accuracy test performed by verifying the activity of two additional 1 & 2 cm loading devices (147.5 & 350.1 kBq) using the calibration factors from table (1). The measured Ra-224 activity is obtained by taking the product of the calibration factor and the γ dose-rates averaged over 3 measurements. A relative error was then evaluated from the GM measured Ra-224 activity and the α-spectrometry measurements from the manufacturer. Relative errors of 13.5%, 0.3%, and 0.3% were found for the 1 cm loading devices using the absorber-only, the absorber & 3D-printed support and 3D-printed-support-only geometries while the relative errors for the 2 cm loading device were found to be 1.1%, -0.5% and 8.3% using the absorber-only, the absorber & 3D-printed support and 3D-printed-support-only geometries respectively.

DISCUSSION AND CONCLUSION

The weak γ-emission of the loading devices makes source verification as recommended by Task Group 53 challenging. Well chambers are the standard instruments to verify seed activity in the mCi range for LDR brachytherapy using a current to air-kerma strength calibration factors from a standard lab or ADCL. On the other hand, DaRT seeds in the µCi range have much weaker γ-emission requiring the use of well chambers in the charge mode with integration times over several minutes. **We found Geiger-Müller detectors to be better suited for DaRT quality assurance as their sensitivity gives a stable reading within seconds.** Moreover, loading devices are shipped with an additional protective steel capsule which decreases the γ-emission further by self-attenuation as opposed to other DaRT applicators. We found a ~50% decrease in signal when the devices were measured without their protective steel capsule which was not a significant factor as long as the devices were measured relatively early in their decay curve (i.e. at the time of reception). The γ dose-rate to Ra-224 activity calibration factors were found to be slightly different between the 1 cm and 2 cm loading devices due to the different alignment of the seeds' center of masses with the GM detector's pancake probe. **The precision of the calibration factors was improved by ~70% with the use of a 3D-printed support that provided stability to the geometry of the setup. Finally, better accuracy (relative error < ~5%) was obtained when using an absorber material to remove low-energy gammas subject to attenuation. We suggest using the 5 mm galvanized steel shielding that comes standard with the shipping package from Alpha Tau Medical Ltd. to build a setup that can be replicated in other centers.**

DISCLOSURES

This work was performed as part of a clinical study funded by Alpha Tau Medical Ltd. (Tel Aviv, Israel). The authors also acknowledge funding from the National Research Council Canada, TransMedTech and Medtech institutes. **We are actively recruiting talented students interested in diffusing alpha-emitters radiation therapy (DaRT) for several graduate research projects.**

REFERENCES

1. Siegel R.L. *et al.*, *Cancer statistics*, CA: a cancer journal for clinicians 69 (1), 7-34, 2019.
2. Sun S. *et al.*, *Endoscopic ultrasound-guided interstitial brachytherapy of unresectable pancreatic cancer: results of a pilot trial*, Endoscopy 38 (04), 399-403, 2006.
3. Jin. Z. *et al.*, *Endoscopic ultrasonography-guided interstitial implantation of iodine 125-seeds combined with chemotherapy in the treatment of unresectable pancreatic carcinoma: a prospective pilot study*, Endoscopy 40 (04), 314-320, 2008.
4. Arazi L. *et al.*, *Treatment of solid tumors by interstitial release of recoiling short-lived alpha emitters*, Physics in Medicine & Biology 52 (16), 5025, 2007.
5. Popovtzer A. *et al.*, *Initial Safety and Tumor Control Results From a "First-in-Human" Multicenter Prospective Trial Evaluating a Novel Alpha-Emitting Radionuclide for the Treatment of Locally Advanced Recurrent Squamous Cell Carcinomas of the Skin and Head and Neck*, International Journal of Radiation Oncology* Biology* Physics 106 (3), 571-578, 2020.

CONTACT INFORMATION

yuji.kamio.chum@ssss.gouv.qc.ca