Supporting Information

Injectable Silver Nanosensors: *In Vivo* Dosimetry for External Beam Radiotherapy using Positron Emission Tomography

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1. Thorax Phantom Setup Plan

Irradiation of the thorax phantom was performed by using two different Ag-nanosensor configurations where Ag-nanosensor #1-4 was used in the first configuration (I) and Ag-nanosensor #5-8 was used in the second configuration (II) (Table S1). Each dose level was irradiated and measured with the PET/CT three times. Delay between individual irradiations was minimum 24h equal to 60.1 half-lives of ^{106}Ag to prevent carry-over of radioactivity. In total 45 individual measurements were conducted, which were divided into 36 of Ag-nanosensors and 9 of the control gel.

Table S1: Experimental plan with gels configuration.

Scan\Dose [Gy]	2	10	22
1	I	II	I
2	I	II	I
3	II	I	II

2. Statistical Analysis

2.1 Ag-Nanosensor Variance Analysis

To analyze possible effects of the individual gels, the position in the phantom, and the irradiated dose, a model with second order interactions was considered:

$$M1: \quad Y_{ijkv} = \mu + pos_i + gel_j + dose_k + \{pos \cdot gel\}_{ij} + \{pos \cdot dose\}_{ik} + \{gel \cdot dose\}_{jk} + \epsilon_{ijkv}$$

Where Y_{ijkv} was the measured activity of position *i*, gel *j*, dose *k* and repetition v. ϵ_{ijkv} was the error and μ the overall mean. Backwards elimination was performed down to the model only including main effects:

$$M2: \quad Y_{ijkv} = \mu + pos_i + gel_j + dose_k + \epsilon_{ijkv}$$

Then a testing of the main effects was performed, down to having only the dose included, as the hypothesis was, that the activity measured was only dependent on the irradiated dose:

$$M3: \quad Y_{ijkv} = \mu + dose_k + \epsilon_{ijkv}$$

$$M4: \quad Y_{ijkv} = dose_k + \epsilon_{ijkv}$$

Normality was evaluated by inspecting the residual/quantile plots. To test for equal variance the Levene's test was used [1].

Nothing suspicious was found in the residual/quantile plots and normality was accepted. Using Levene's test for equal variance[1], the four dose levels 0-, 2-, 10- and 22 Gy, were found to have equal variance P=0.0989. Please note that the dose was not completely homogeneous within each group, so equal variance was accepted.

Four models were considered M1-M4 (see equations above), ranging from complex to very simple (Table S2).

Table S2. Statistical analysis of results for each model. DF: Degrees of Freedom, RSS: Residual sum of squares, MS: Mean squared error, F: F-test value

Model	No. par.	DF	RSS	MSE	F	P(F>f)	R^2
M1	19	26	0.00247935	0.00009536			0.9932
M2	11	34	0.00297182	0.00008741	0.645	0.733	0.9916
M3	2	43	0.00643799	0.00014972	4.406	0.001	0.9825
M4	1	44	0.00676092	0.00015366	2.157	0.149	0.9816

The step from M1 to M2 was not significant. The step from M2 to M3 was significant, however the decrease in R^2 was miniscule. Taking statistical methodology very literally, one should thus accept M2. The step from M3 to M4 was also not significant. Since the decrease in variance explained were so small, we choose to accept the simplest possible model M4 as it still maintains a R^2 of 0.9816. This can be interpreted as the activity measured can be adequately explained by the effective dose alone and that position in the phantom and the individual gels has a negligible effect.

To evaluate the error the irradiated dose was calculate from the activity using the model, which was grouped into the four dose levels (Table S3).

Table S3: Error in calculated dose

Dose group [Gy]	Standard deviation [Gy]	Maximum lower error [Gy]	Maximum upper error [Gy]
0	0.927	-1.905	1.161
2	0.612	-1.419	0.822
10	0.963	-1.543	2.189
22	1.575	-2.462	3.606

References

[1] M. B. Brown and a B. Forsythe, “Robust Tests for Equality of Variances,” *J. Am. Stat. Assoc.*, vol. 69, no. 346, pp. 364–367, 1974.