Supplementary Materials

Table S1. P1_1 activity, NLV and PTV dose-volume values. In bold and italic, the optimal balance between the minimum PTV 80 Gy dose threshold and the maximum NLV 70 Gy dose threshold is represented.

Activity (GBq)	NLV ratio	NLV (ml)	NLV mean dose (Gy)	NLV median dose (Gy)	PTV ratio	PTV (ml)	PTV mean dose (Gy)	PTV median dose (Gy)
0.000	1.000	1245	0.0	0.0	0.000	0.0	0.0	0.0
0.250	1.000	1245	5.6	4.8	0.000	0.0	12.1	10.3
0.500	1.000	1245	11.2	9.5	0.001	0.2	24.2	20.6
0.750	0.998	1242	16.7	14.3	0.069	16.6	36.3	30.9
1.000	0.993	1236	22.3	19.0	0.146	35.3	48.4	41.2
1.250	0.975	1214	27.9	23.8	0.216	52.2	60.5	51.5
1.500	0.938	1168	33.5	28.5	0.321	77.3	72.6	61.8
1.750	0.892	1110	39.1	33.3	0.427	103.0	84.7	72.1
2.000	0.841	1047	44.6	38.0	0.519	125.1	96.8	82.4
2.250	0.791	984	50.2	42.8	0.596	143.6	108.9	92.7
2.500	0.739	920	55.8	47.5	0.658	158.6	121.0	103.0
2.598	***0.719***	***895***	***57.9***	***49.4***	***0.680***	***163.9***	***125.7***	***107.0***
2.750	0.688	856	61.4	52.3	0.710	171.1	133.1	113.3
3.000	0.639	796	67.0	57.0	0.751	181.0	145.2	123.6
3.250	0.587	731	72.6	61.8	0.783	188.8	157.2	133.9
3.500	0.535	666	78.1	66.6	0.812	195.8	169.3	144.1
3.750	0.487	607	83.7	71.3	0.836	201.5	181.4	154.4
4.000	0.444	553	89.3	76.1	0.856	206.3	193.5	164.7
4.250	0.404	503	94.9	80.8	0.872	210.2	205.6	175.0
4.500	0.368	459	100.5	85.6	0.886	213.6	217.7	185.3
4.750	0.334	416	106.0	90.3	0.898	216.6	229.8	195.6
5.000	0.303	378	111.6	95.1	0.910	219.3	241.9	205.9
5.250	0.275	343	117.2	99.8	0.921	222.0	254.0	216.2
5.500	0.250	312	122.8	104.6	0.930	224.3	266.1	226.5
5.750	0.227	283	128.4	109.3	0.938	226.1	278.2	236.8
6.000	0.207	258	133.9	114.1	0.945	227.7	290.3	247.1
6.250	0.189	235	139.5	118.8	0.951	229.1	302.4	257.4
6.500	0.173	215	145.1	123.6	0.956	230.4	314.5	267.7
6.750	0.159	198	150.7	128.3	0.961	231.5	326.6	278.0
7.000	0.146	182	156.3	133.1	0.965	232.6	338.7	288.3
7.250	0.135	168	161.9	137.9	0.969	233.5	350.8	298.6
7.500	0.124	155	167.4	142.6	0.973	234.5	362.9	308.9
7.750	0.116	144	173.0	147.4	0.976	235.2	375.0	319.2
8.000	0.108	134	178.6	152.1	0.979	236.0	387.1	329.5
8.250	0.100	125	184.2	156.9	0.982	236.6	399.2	339.8

Activity (GBq)	NLV ratio	NLV (ml)	NLV mean dose (Gy)	NLV median dose (Gy)	PTV ratio	PTV (ml)	PTV mean dose (Gy)	PTV median dose (Gy)
8.500	0.094	117	189.8	161.6	0.985	237.3	411.3	350.1
8.750	0.088	109	195.3	166.4	0.986	237.7	423.4	360.4
9.000	0.082	103	200.9	171.1	0.988	238.1	435.5	370.7
9.250	0.077	96	206.5	175.9	0.989	238.4	447.5	381.0
9.500	0.073	91	212.1	180.6	0.990	238.7	459.6	391.3
9.750	0.069	86	217.7	185.4	0.992	239.1	471.7	401.6
10.000	0.065	81	223.2	190.1	0.993	239.3	483.8	411.9
10.250	0.062	77	228.8	194.9	0.994	239.5	495.9	422.2
10.500	0.058	72	234.4	199.7	0.995	239.8	508.0	432.4
10.750	0.055	68	240.0	204.4	0.996	240.0	520.1	442.7
11.000	0.052	65	245.6	209.2	0.996	240.2	532.2	453.0
11.250	0.050	62	251.2	213.9	0.997	240.3	544.3	463.3
11.500	0.047	59	256.7	218.7	0.998	240.5	556.4	473.6
11.750	0.045	56	262.3	223.4	0.998	240.6	568.5	483.9
12.000	0.042	53	267.9	228.2	0.998	240.7	580.6	494.2

Note: This table shows the expected NLV and PTV mean and median doses, the volumes (NLV and PTV) comprising the dose threshold imposed (NLV < 70 Gy, PTV > 80 Gy) and respective ratios (NLV ratio and PTV ratio) as a function of the ^{90}Y activity to be administered. Based on the same dose thresholds, the optimal ^{90}Y activity would be 2.598 GBq, the mean and median absorbed doses respectively 57.9 Gy and 49.4 Gy in the NLV and 125.7 Gy and 107.0 Gy in the PTV. This way, 71.9% of voxels (i.e., 895 ml) in NLV and 68.0% (i.e., 163.9 ml) in PTV end up, respectively, below 70 Gy and above 80 Gy.

Table S2. Comparison of the mean and median doses in NLV and PTV, estimated with: (i) the standard formula of the glass MS manufacturer's protocol, and (ii) the optimized methodology considering the minimum PTV 80 Gy dose threshold and the maximum NLV 70 Gy dose threshold.

	Manufacturer's protocol					Optimized methodology				
Case study	**Administered activity (MBq)**	**NLV mean dose (Gy)**	**NLV median dose (Gy)**	**PTV mean dose (Gy)**	**PTV median dose (Gy)**	**Optimal activity (MBq)**	**NLV mean dose (Gy)**	**NLV median dose (Gy)**	**PTV mean dose (Gy)**	**PTV median dose (Gy)**
P1_1	2750	61.3	52.2	133.0	113.2	2598	57.9	49.4	125.7	107.0
P2_2	3347	78.2	68.1	111.8	98.7	3748	87.5	76.3	125.2	110.6
P3_3	3961	73.0	42.7	92.9	78.9	6239	115.0	67.2	146.4	124.3
P4_5	4231	25.0	9.4	89.3	88.1	10662	62.9	23.6	225.0	222.1
P5_6	4305	90.5	52.8	134.6	99.8	4397	92.4	54.0	137.5	102.0
P6_7	2814	74.0	67.6	130.5	129.6	2274	59.8	54.6	105.5	104.8
P7_8	5604	74.4	70.3	94.2	94.4	8094	107.4	101.6	136.0	136.4
P8_9	1537	24.1	0.4	94.5	91.9	4898	76.9	1.4	301.3	292.8
P8_10	4227	67.1	63.0	117.7	95.8	2219	35.2	33.1	61.8	50.3
P10_12	1992	70.4	64.7	97.6	88.4	1471	52.0	47.8	72.1	65.3
P12_14	4481	31.2	9.4	151.5	106.9	8675	60.4	18.2	293.2	207.0

Note 1: For each case study, the optimal activity was determined by the global maximum of the objective function. In some cases (e.g., P7_8, P8_10, and P10_12) it would be more appropriate to choose a local maximum of the objective function rather than the global maximum. In any case, the optimized methodology must always be supervised taking into account clinical criteria, absorbed dose constraints on PTV and NLV, and other parameters that are the responsibility of the physician. In this regard, dosimetric supervision can be done based on dose-volume data as in Table A1 or using dose-volume histograms.

Note 2: These results indicate that the median is more suitable for characterizing the absorbed dose distribution in PTV and NLV than the mean.