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Letter to the Editor

Dose rate *does* matter in endovascular brachytherapy

Dear Editor-in-Chief,

In a recent letter, Das and Peters [1] have made the suggestion that dose rate is not an important factor in determining the effectiveness of endovascular brachytherapy. As we [2–4] and others [5] have argued earlier, we suggest here that the dose rate or, equivalently, the treatment time, *is* important.

Das and Peters [1] correctly argue that if the irradiation time is much shorter than characteristic time for repair of "sublethal" damage, the dose rate will not matter, because there will be very little repair taking place during the treatment. The corollary, of course, is that if the irradiation time is not smaller than the characteristic repair time, dose rate will matter, with longer irradiation times resulting in reduced biological effects, because of sublethal damage repair during the irradiation.

However, the implications of this argument depend on the actual value of the appropriate damage repair halftime. In their calculations, Das and Peters [1] used a repair halftime of 90 min, which is long compared with typical endovascular brachytherapy irradiation times, both for $^{90}Sr/^{90}Y$ sources (irradiation time typically <5 min), and also for ^{192}Ir sources (irradiation time typically 20–35 min). Ergo, no dose-rate effects.

However, the 90-min repair halftime that Das and Peters [1] uses is unrealistically long. Indeed, back in 1984, it was Peters et al. [6] who first provided quantitative data showing that repair halftimes for acutely responding normal tissues in vivo were less than 1 h, reporting measured values ranging from 18 to 54 min. This was in contrast to possibly longer times in late-responding vascular tissue, where values of the order of 90 min may indeed be appropriate [6]. Das and Peters [1] have applied here parameters relevant to late-occurring vascular damage. However, this is not pertinent to the endpoint of relevance here, which is radiation-induced reduction or prevention of restenosis—an acute response.

The animal results suggesting that repair halftimes for acutely responding normal tissues are <1 h [6] have since been corroborated by in vitro data from cells of human origin. An analysis [7] of in vitro dose-rate studies in 36 cell lines of human origin (mean repair halftime 32 min) includes a subanalysis of 6 cell lines derived from normal human tissues (mean repair halftime 22 min). Later studies with human aortic smooth muscle cells (repair halftime 30 min [4]) and porcine smooth muscle cells [5] also support the conclusion that an appropriate repair halftime here is about 30, not 90 min.

A repair halftime of 30 min is still much longer than typical $^{90}Sr/^{90}Y$ beta irradiation times, so dose rate would not be important there, but 30 min is comparable to typical irradiation times with ^{90}Ir gamma rays. For example, the recent SCRIPPS trial [8] used an exposure time of about 35 min. In this case, the decrease in the effective dose (compared to that for a very short exposure) as estimated using the (as we argue) unrealistic parameters of Das and Peters ($T_{1/2}=90$ min, $\alpha/\beta=3$ Gy [1]) is 7%—small enough, perhaps, to argue that dose rate is not so important. However, using parameters more appropriate for early-responding damage ($T_{1/2}=30$ min, $\alpha/\beta=8$ Gy), this reduction in effective dose is 16%, no longer such a small correction.

Of course all that needs to be done is to appropriately increase the dose to take into account the decreased effect with increasing treatment time—but this *should* be done when treatment times are greater than about 10 min.

References

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David J. Brenner
Eric J Hall
Center for Radiological Research
Columbia University, 630 West 168th Street
New York, NY 10032, USA
Tel.: +1-212-305-9930
Fax: +1-212-305-3229
E-mail address: djb3@columbia.edu