Supplemental Appendix A

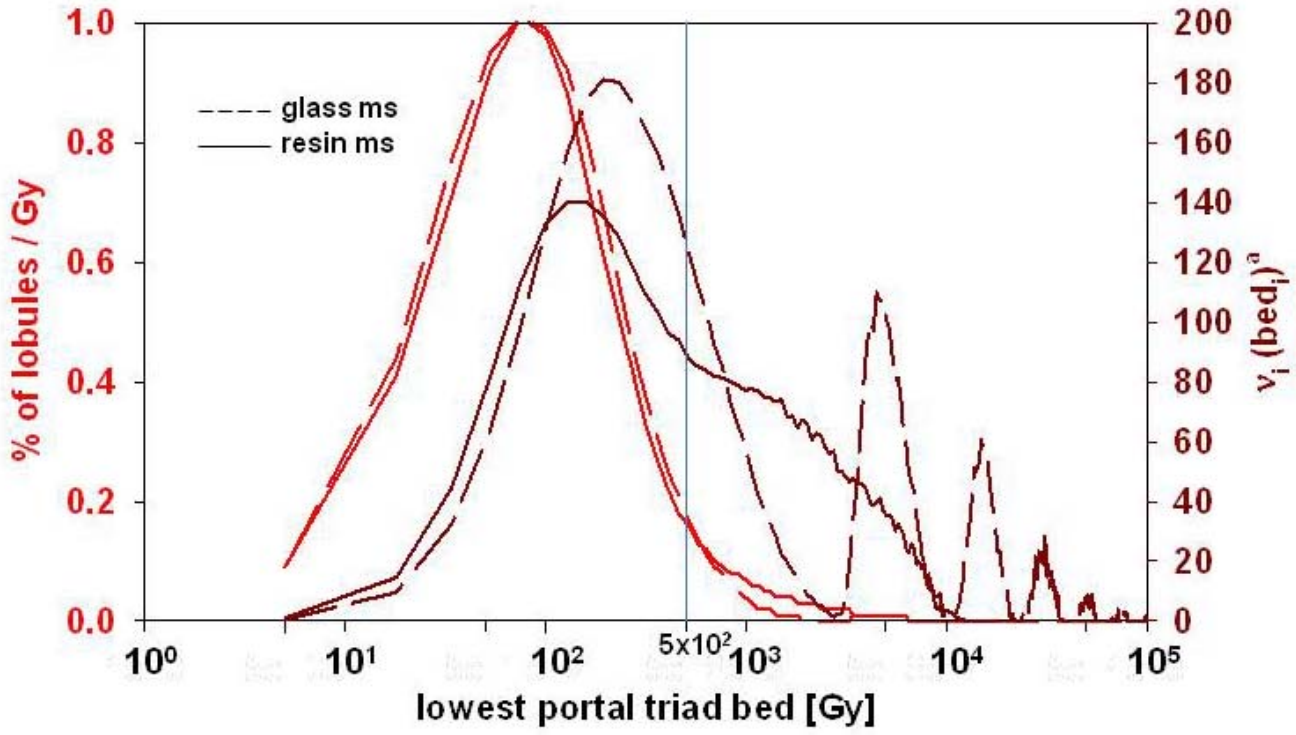
The results show that although the EUD_{KB} formalism correctly described the toxicity risk in partial-liver-volume EBRT, for which the dose was uniform in the targeted liver volume (Table 1), it failed to explain the toxicity risk in liver radioembolization, for which the observed BED_{50} resulted in EUD_{KB50} about 5-fold higher than in EBRT (Table 1).

This result arises from the incorrect treatment of high doses in the EUD_{KB} formalism. A BED higher than 200 Gy delivered to a lobule will definitely kill the lobule. Thus, all BED values higher than 200 Gy delivered to one lobule should contribute similarly to the EUD_{KB}. Such is not the case using a microscale dose distribution. Supplemental Figure 1 clearly shows that lobules that trapped several microspheres and whose portal triads received a BED higher than 500 Gy contributed significantly to the EUD_{KB} although they represented a minor lobule fraction not critical for liver recovery. Only a single lobule with a BED $\rightarrow \infty$ results in a liver $EUD_{KB} \rightarrow \infty$ when $a > 0$ ($a = 1.06$). Even for $a < 0$, this issue would not be resolved, as in that case only a single element having a BED ≈ 0 results in a tissue $EUD_{KB} \approx 0$. These two limits clearly show that the EUD_{KB} formalism is not adaptable to microscale dose distributions.

Supplemental Appendix B

The EUD_{JH} formalism succeeded in giving a similar EUD_{50} for the dose toxicity risk observed in whole-liver EBRT and in resin or glass microsphere radioembolization. However, the EUD_{JH} formalism failed in predicting the different BED_{50} values observed in partial-liver-volume EBRT, resulting in a drop in EUD_{JH50} by 11 Gy when preserving a third of the liver volume from radiation.

This result arises from the fact that a hepatic lobule is not a unique cell but a functional subunit, that is, a real tissue requiring the cooperation of all its cells to work and survive. As a result, the lobule survival fraction is not described by an exponential curve; instead, the dose–failure risk relationship of a lobule should exhibit a sigmoid shape as do all organs.



Supplemental Figure 1. Dose contribution to EUD. Red lines: simulated total lobule fractions as a function of the minimal BED delivered to their 6 portal triads derived for the resin (solid lines) and glass (dashed lines) microspheres. Brown lines: contributions to the EUD as a function of the lobule dose bed. Although the lobules receiving more than 500 Gy to their portal triads represent a minor fraction, their contribution to the EUD is significant.