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COMMENT

Comment on 'Monte Carlo simulation on a gold nanoparticle irradiated by electron beams'

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Abstract

A recent paper by Chow *et al* (*Phys. Med. Biol* **57** 3323–31) quantifies the dose due to secondary electrons created by gold nanoparticles when irradiated by electron beams. That paper fails to compare this dose to the overall dose from the electron beam. EGSnrc calculations are performed to show that, even for the unrealistically favourable case presented by Chow *et al* of a very narrow electron beam directed only at the nanoparticle, the dose outside the nanoparticle due to the secondary electrons generated by the nanoparticle is negligible compared to the dose from the primaries. Thus, it is irrelevant whether the dose from secondary particles is enhanced by the nanoparticles or not and there appears to be no advantage to using gold nanoparticles in electron beams, unlike the case for photon beams.

In a recent paper, Chow *et al* (2012) quantified the excess dose due to secondary particles created in gold nanoparticles when irradiated by a pencil beam of electrons incident on the nanoparticle centred in a small water voxel. I fail to see how the reported calculations are of any relevance. Even if we accept the premise of a 100 nm diameter beam of electrons incident on the nanoparticle, then a relevant question to ask is: How large is the dose from the secondary electrons generated in the gold nanoparticle relative to the dose delivered by the beam itself? Chow *et al* (2012) explicitly state that this concern is beyond the scope of their study, and in their close-to-concluding statement point out that 'there is little advantage to using an electron source in combination with gold nanoparticle when compared to a photon source'. However, the mere existence of their detailed study suggests that there is some advantage, whereas a simple consideration of the ratio of the extra dose from nanoparticle-generated secondaries to the total dose would show that all of the issues studied are not relevant.

As shown below, even for the extremely narrow electron beams modelled by Chow *et al* (2012), multiple scattering in a minimal amount of surrounding material causes the beam to spread out and contribute primary dose to the region around the nanoparticle and this dose completely overwhelms the excess dose from the nanoparticle.

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I have repeated their calculations using the EGSnrc system (Kawrakow 2000, Kawrakow *et al* 2011). The calculated results are a complex interplay between many parameters and not all of these parameters are specified explicitly in the original paper, nor are statistical uncertainties given anywhere. Calculations are performed here for a 4 MeV beam since it will spread out the least when passing through the micro-phantom and thus be most favourable to the Chow *et al* (2012) argument. A 100 nm gold nanoparticle is placed at the centre of a minimal micro-phantom which extends to twice the mean effective range of the nanoparticle-generated secondaries as given by Chow *et al* (2012) for the 4 MeV case, namely 32 μm. This ensures that almost all of the energy from the secondaries from the gold nanoparticle is deposited in the volume. This small volume was necessary because when a 1.5 mm cubic voxel was used, as implied in Chow *et al* (2012), even in a narrow beam with 5×10^9 electrons incident on the voxel (20 times the number of histories in Chow *et al* (2012)), the statistical uncertainty on the dose from the nanoparticle-generated secondaries was greater than 25%. This is because, for a 100 nm diameter beam, the fluence of particles actually reaching the nanoparticle region centred at 0.75 mm depth in a 1.5 mm cubic voxel is less than 1 part in 10^6 of the incident fluence, the rest being scattered laterally out of the very narrow beam. Chow *et al* (2012) appear to have avoided this issue by making the electron beam start on the nanoparticle's surface, but this is even less realistic than using the 32 μm micro-phantom used here, already a very unrealistic model which is very favourable to seeing any nanoparticle dose enhancement.

The current calculations are for a cylindrical geometry with a cylindrical nanoparticle of diameter and length 100 nm. These EGSnrc calculations define a secondary electron as any electron produced in the nanoparticle region after a Moller interaction or via atomic relaxation (electron impact ionization leading to Auger or Koster Kronig electrons or fluorescent photons which then create a secondary electron) or bremsstrahlung photons created in the nanoparticle which later create a secondary electron. The Moller-generated secondaries provide a significant majority of the excess dose from secondaries. For this situation, when simulating 2.5×10^8 incident electrons, the ratio of the total energy deposited outside the nanoparticle region by these secondaries versus the energy deposited by secondaries from that region when water replaced the nanoparticle is 9.5 ± 0.5. This value should be comparable to the value of 4.5 given with no uncertainty by Chow *et al* (2012). The differences may be due to inclusion of different processes in the present analysis, or a difference in lower energy cutoffs (1 keV in the current calculations, but unspecified by Chow *et al* (2012)) or differences in the exact geometries considered or more fundamental differences in how the two codes deal with such very small regions. In practice, EGSnrc will be in single scattering mode for electron transport in such very small regions. The 1 keV cutoff, which is the low-energy limit in EGSnrc, is slightly high since the range of 1 keV electrons in water is about 40 nm. Also this means that the Auger electrons in water are not modelled since their energy is below 1 keV. If these were included by Chow *et al* (2012), they might reduce the 9.5 ratio reported above. However, this detail will not change the major conclusion being drawn below.

The main result is that the dose delivered by the secondaries created in the nanoparticle is a completely negligible fraction of the total dose delivered near the nanoparticle, even when we talk about this incredibly narrow beam focused directly on the nanoparticle from a distance of 32 μm. The total energy deposited in the water outside the nanoparticle region either filled with gold or water is the same to four significant figures in the EGSnrc calculations. The nanoparticle does scatter electrons more widely so the total energy deposited directly behind the nanoparticle decreases by 9%. This energy is deposited slightly laterally. Even in this unrealistic situation of a nanobeam directed only at the nanoparticle and only passing through a 32 μm layer of water, the energy deposited outside the nanoparticle by the secondaries

generated in the nanoparticle is 6.5×10^{-5} of the total energy deposited in this micro-phantom. In any realistic situation, there will be a broader beam of electrons, the vast majority of which will not interact with any nanoparticle at all and hence the ratio of the dose from secondaries from the nanoparticle to the total dose will decrease even more.

But what about the energy deposition immediately adjacent to the nanoparticle rather than the broader region (32 μm) over which the secondaries deposit excess energy? If we consider a 150 nm radius beam on a nano-phantom with 100 nm around the nanoparticle (nano-phantom radius 150 nm, depth 300 nm), then the ratio of the total energy deposited in the water outside the nanoparticle to that when there is only water is $1.009 \pm 0.1\%$. These dimensions are comparable to those of DNA. If we make the phantom somewhat larger, comparable to a cell's size (radius 10 μm, height 20 μm), and have an electron beam that just irradiates the cell, the total energy deposited within 100 nm of the nanoparticle has only increased by $(0.9 \pm 0.3)\%$.

In view of these results, the discussion of the details of the excess dose when using nanoparticles in electron beams seems inappropriate because this dose is completely negligible compared to the dose from the primary electrons. Nanoparticles in photon beams create a significant dose enhancement because the vast majority of photons do not interact in any given small region of normal tissue and a far greater fraction interacts when there are nanoparticles present. This is because the cross section per cm is roughly 600 times higher for gold than that for water. Electron beams interact more or less continuously in any material they pass through, so based on the considerations above, nanoparticles offer no advantage in electron beams, unlike the case in photon beams.

References

Chow J C L, Leung M K K and Jaffray D A 2012 Monte Carlo simulation on a gold nanoparticle irradiated by electron beams *Phys. Med. Biol.* **57** 3323–31

Kawrakow I 2000 Accurate condensed history Monte Carlo simulation of electron transport: II. Application to ion chamber response simulations *Med. Phys.* **27** 499–513

Kawrakow I, Mainegra-Hing E, Rogers D W O, Tessier F and Walters B R B 2011 The EGSnrc Code System: Monte Carlo simulation of electron and photon transport *NRC Technical Report* PIRS-701 v4-2-3-2 (Ottawa, Canada: National Research Council) http://www.irs.inms.nrc.ca/inms/irs/EGSnrc/EGSnrc.html