PriMera Scientific
Medicine and Public Health
Volume 7 Issue 4 October 2025
ISSN: 2833-5627

Recent Developments in Quantum Biology Identifies the best Ions for Curative Radiation Oncology

Type: Editorial Note
Received: September 18, 2025
Published: October 04, 2025

Citation:
Anders Brahme. "Recent Developments in Quantum Biology Identifies the best Ions for Curative Radiation Oncology". PriMera Scientific Medicine and Public Health 7.4 (2025): 28-30.

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It has been known for many years that the last few radiation therapy treatment fractions can increase the tumor cure from a few percent to 80-90 % with classical photon or electron beam treatments [1, 2]. This is indicating that the loss of the last few clonogenic tumor cells are determining the therapeutic outcome and the probability of cure. Interestingly, this also means that both the *therapeutic beams and the tumor are Quantized* and the treatment outcome is largely dependent on the probability that *all tumor clonogens are lethally hit* by the *particles of the therapeutic beam* weather they are primary electrons or secondary electrons in photon and ion beams. In fact, it has recently been demonstrated that the therapeutic entity of most if not all radiation beams is the low energy secondary so called δ -electrons or δ -rays of energy below ≈1 keV that are capable of delivering a local dose of about 1M Gy to 10 nm size objects. Such critical energy deposition sites are the periphery of the nucleosome and δ -rays can induce a very severe *Dual Double Strand* Break (DDSB) on their DNA as it is wound two turns around the nucleosome [3]. Unfortunately, this kind of damage is very hard to handle by the most common DNA repair system for DSB´s, namely the Non Homologous End Joining process (NHEJ) as the resulting DSB´s are as close as 80 base pairs or 35 nm from each other. The two DNApk molecules needed for repair dose not generally have room enough for each other to work on the DNA [3, 4]. Even if the damage sometimes can be repaired by a switch to the Homologous Recombination DSB repair machinery, this is one of the most severe damage events to nuclear DNA that may often lead to cell death [3, 4]. The interesting fact that the these δ -rays are produced by practically all therapeutic beams and it make them the key Effectors of all curative radiation therapy as discussed in further details recently [3-7]. As proven in some of these studies [4, 7] the Relative Biological Efficiency of light ion beams is closely related to the mean δ -ray multiplicity along the ion track as they are produced new almost as fast as they are absorbed along the track. The RBE in front of the Bragg peak of Boron, Carbon and Nitrogen ions is about 3, corresponding to ≈3 δ -rays in average along every section of these high ionization density ion tracks.

Since there is only a few viable clonogenic cell left in the tumor during the last week of a curative treatment it is unsuitable to try to use high ionization density ions to hit them. This is so even if they generally are our sharpest tool available to treat malignant tumors, but only if we know precisely where the clonogens are and where to aim the beam to hit the cell nuclei, but also if there are so many cells that their exact locations is unimportant! In fact, if we know precisely where e.g. 2***n*** cells are located we need just ***n*** ions since each ion can hit at least 2 cells in one shot when we know where

they are! If we don't, according to Heisenberg's wonderful thinking, applied on this simplistic case, we need a beam at least as large as the tumor if we wish to be sure to hit them all (actually a little bit bigger if there is also uncertainties in the beam patient set up [8]) and not least we need also to consider the quantum biology of curative radiation therapy so we don't get a *microscopic ion beam cold spots* on some of the clonogens. However, at the beginning of a treatment with millions of hypoxic radiation resistant tumor cells, ion beams are the most effective treatment since independent of where we aim the ions, we will hit thousands of tumor cells. If you have an ion path through millions of cells its effect on the tissue is well described by the dose averaged pencil beam dose distribution as it is the average response that counts and it is given by taking the average effect on the millions of cells which is exactly the definition of the mean dose distribution of the beam over cell nuclear sizes! If there is only a few clonogens left such a mean energy deposition kernel is too crude, and we have to look at the probability that at least one of the remaining clonogens is missed by the beam and may repopulate the tumor [9]! And today we know very well that this may happen since caspase 3 is likely to step in after the treatment trying to recover normal tissue homeostasis after the treatment inducing accelerated repopulation which is known to also affect possibly remaining tumor clonogens [9].

As discussed in a previous communication [5, 10] the low and high dose apoptosis makes the optimal daily fractionation window being at about 2 Gy/Fr of low ionization density high energy electrons or photons to minimize normal tissue damage for a given dose to the underlying tumor as proven by ≈80 years of radiation therapy experience. Fortunately, at this dose level there is approximately only a single DDSB induced in normal tissues so we should not go to higher doses to spare them from high ionization density DDSB! For ions this requires that the ionization density in the entrance or plateau region should also be as low as possible to retain the clinically established fractionation window also for light ions! The best way to achieve this is by using the lightest ions from Helium and Lithium to Boron as these ions has lower biological effectiveness both in the plateau and fragmentation tail regions without losing much of their effectiveness in the Bragg peak [4]. Actually Carbon ions have higher apoptotic and senescent responses per unit dose some 5 cm in front of the Bragg peak than at the Bragg peak itself which is undesirable as it very often affects normal tissues [4]. At the same time these light ions also reduces the risk for microscopic cold spots in the tumor as high ionization density is linked to a reduced probability for cure at high doses [5]. In fact, the higher the ionization density along the ion track the higher is the local δ -ray multiplicity and biological effect and thus the microscopic heterogeneity is higher (as the dose is close to zero between ions) requiring still higher absorbed doses to counteract the increased risk for microscopic cold spots on tumor clonogens. This results in a decreased dose response slope of heavier ion beams and at the same time an increased early risk of normal tissue damage and reduced cure at high doses and will thus result in an unnecessarily reduced complication free cure [4-7]! One way to get rid of them would be to use a deterministic *microscopically uniform ion grid* in the form of a 7*m*m step size perfect hexagonal grid, but it is not so easy to make [4]. Therefore, treatments with Carbon and heavier ions would benefit by delivering the last 10 to 15+ Gy-Equivalent dose by low ionization density electrons or photons resulting in a steeper dose response due to high microscopic uniformity, a reduced normal tissue damage, better tumor cure and thus an improved complication free cure [5, 7]! In conventional thinking the few remaining tumor clonogens may not even be so hypoxic that they need a high ionization density then and we could avoid microscopic cold spots and get a steep dose response slope with improved complication free cure by such a *low ionization density treatment roundup*! This means that the higher ionization densities that are presently contemplated in Germany and Japan with Oxygen and Neon ions really should be avoided as we already passed the optimal therapeutic ion beam with Carbon ions and even Boron ions may sometimes benefit from such a low ionization density roundup for example when treating close to sensitive organs at risk. This conclusion is also in line with the early Neon ion treatments in Berkeley (1970s, [4]) that didn't show sufficient improvements compared to the conventional treatments at the time. We therefore need to use the lightest ions with uttermost clinical care to really benefit from their interesting clinical possibilities ensuring minimal normal tissue damage and maximum complication free cure [4].

References

1. Munro TR and Gilbert CW. "The relation between tumor lethal dose and the radiosensitivity of tumor cells". Brit. J. Radiol 34 (1961): 246-51.
2. Brahme A. "Dosimetric precision requirements in radiation therapy". Acta Radiol. Oncol 23 (1984): 379-391.

3. Brahme A and Lorat Y. "The Dual Double Strand Break: the Key Effector of Curative Radiation Therapy". Biophysica 3 (2023): 668-694.
4. Fundamental Molecular Understanding of Quantum Biology Optimized Curative Radiation Oncology: Identifying Optimal Molecular Tumor Diagnostics, Dose Fractionation and Intensity & Quality Modulated Electron, Photon & Light Ion Beams. Eliva Press, Chisinau, Moldova (2024).
5. Brahme A. "TP53 and the Ultimate Biological Optimization Steps of Curative Radiation Oncology". Cancers 15.17 (2023): 4286.
6. Brahme A. "New Radiation Therapy Optimization Principles Based on recent Developments in Molecular Radiation Biology". Ann Case Rep 9 (2024): 101625.
7. Brahme A. "Improving Radiation Therapy Efficacy Considering DNA Repair, TP53 Mutations, Microscopic Heterogeneity and Low & High Dose Apoptosis". Sub to Frontiers in Oncology (2025).
8. Kaver G., et al. "Stochastic optimization of intensity modulated radiotherapy to account for uncertainties in patient sensitivity". Phys. Med. Biol 44 (1999): 2955-2969.
9. Zhao M., et al. "Caspase-3 knockout attenuates radiation-induced tumor repopulation via impairing the ATM/p53/Cox-2/PGE2 pathway in non-small cell lung cancer". Aging 12 (2020): 21758-21776.
10. Brahme A. "Recent Developments in Molecular Radiation Biology Can Improve Radiation Oncology". PriMera Scientific Medicine and Public Health 6.5 (2025): 19-20.