Using Radiobiology Simulators for Evaluation of $^{99m}$Tc Auger Electrons for Targeted Tumor Radiotherapy

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ABSTRACT: Technetium-$^{99m}$Tc has been widely used as an imaging agent; however, few studies evaluated its potential use as a therapeutic agent. The present study aimed to analyze the potential use of $^{99m}$Tc Auger electrons for targeted tumor radiotherapy by computational methods. Thus, three different computational simulators were used to estimate the yield of DNA damage, the probability of correct repair and cell kinetic effects after irradiation with $^{99m}$Tc electrons, iodine-$^{131}$I beta minus particles and astatine-$^{211}$At alpha particles. Based on the obtained results, it is possible to conclude that $^{99m}$Tc CKMMX (all M-shell Coster-Kroning – CK – and super CK transitions) electrons and Auger MXY (all M-shell Auger transitions) are valuable for targeted tumor radiotherapy.

1 INTRODUCTION

Targeted tumour radiotherapy with Auger electron emitters is an appealing, but challenging approach for systemic radiation therapy. Auger electrons are emitted by approximately half radioisotopes decaying by either electronic capture or internal conversion, including Technetium-$^{99m}$Tc. Over the past decade, $^{99m}$Tc has been widely used as an imaging agent, but few studies have evaluated its potential use as a therapeutic agent. Results already obtained with $^{99m}$Tc are encouraging; nonetheless, the definitive role of $^{99m}$Tc as a therapeutic agent is far from conclusive. A short half-life, stable daughter nuclide, Auger electron energies suitable for target tumour radiotherapy and ability to do in vivo imaging are some potentially advantageous characteristics of $^{99m}$Tc (Tavares et al. 2010a). The present study aimed to analyze the potential use of $^{99m}$Tc Auger electrons for targeted tumour radiotherapy by computational simulation.

2 METHODS

Three different computational simulators were used to estimate the yield of DNA damage - fast Monte Carlo damage algorithm (MCDS), the probability of correct repair - Monte Carlo excision repair algorithm (MCER), and cell kinetic effects - virtual cell radiobiology algorithm (VC), after irradiation with $^{99m}$Tc electrons, iodine-$^{131}$I beta minus particles and astatine-$^{211}$At alpha particles (Semenenko & Stewart 2004, Stewart 2004, Semenenko et al. 2005, Semenenko & Stewart 2005).

3 RESULTS

The percentage of simple- and double-strand breaks after irradiation, calculated using the MCDS simulator, was always higher for $^{99m}$Tc CKMMX (all M-shell Coster-Kroning – CK – and super CK transitions) electrons and Auger MXY (all M-shell Auger transitions) than that for $^{131}$I beta minus particles and was similar to $^{211}$At alpha particles. An analogous trend was observed for the percentage of complex single- and double-strand breaks. Besides, the remaining $^{99m}$Tc electrons obtained by internal conversion were less able to induce DNA damage, which may be explained by the higher tissue range of these $^{99m}$Tc electrons, whose behaviour is similar to beta minus particles (low LET particles). Results from MCER simulator showed that regardless the repair process used, the probability of correct repair of single-strand breaks is lower for $^{99m}$Tc CKMMX electrons and Auger MXY than that for $^{131}$I beta minus particles and is comparable to $^{211}$At alpha particles. Furthermore, probability of conversion to DSBs was higher for $^{99m}$Tc CKMMX electrons and Auger MXY than that for $^{131}$I beta minus particles and is comparable to $^{211}$At alpha particles. VC simulator main findings showed that: 1) $^{99m}$Tc CKMMX electron and Auger MXY had a higher probability of inducing mutagenesis and genetic instability than $^{131}$I beta minus; 2) $^{131}$I beta minus par-
articles were the most likely of all the irradiating agents studied to induce neoplastic transformation; and 3) 99mTc CKMMX electron and Auger MXY had a higher ability to induce lethal damage, due to mutations, than the other particles studied. This suggests that the higher probability of induced mutagenesis and enhancement of genetic instability of 99mTc CKMMX electron and Auger MXY will potentially lead to cell death or benign mutations and not to neoplastic transformation (Tavares et al. 2010b).

4 CONCLUSIONS

99mTc electrons CKMMX and Auger MXY present a therapeutic potential comparable to high linear energy transfer 211At alpha particles and higher than beta minus particles of 131I, while all remaining 99mTc electrons have a therapeutic potential similar to 131I beta minus particles. Additionally, apoptosis induction probability was found to be higher for 99mTc electrons CKMMX and Auger MXY than 131I beta minus particles and similar to 211At alpha particles. Based on the obtained results, one can conclude that 99mTc CKMMX electrons and Auger MXY are valuable electrons for targeted tumor radiotherapy.

5 REFERENCES

Stewart, R. 2004 Computational Radiation Biology Purdue University, School of Health Sciences, West Lafayette