Proton radiography of cells administered with gold nanoparticles

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Introduction

Radiopaque materials are commonly used to enhance radiographic contrast. Gold nanoparticles are a new type of contrast agent, providing a very small size and a high atomic number (Z=79). As they have a radiosensitizing effect [1] they are not only beneficial for radiodiagnostics but turn out to be very valuable in radiotumortherapy. They enable a better delineation of the tumor and also amplify the effect of X-irradiation. To investigate whether gold nanoparticles are also applicable as a contrast agent for high energy particle radiation, they were incorporated in CHO (Chinese Hamster ovary) cells which were irradiated with a proton beam. Further tests have been performed to investigate, whether gold nanoparticles show a radiosensitizing effect with Carbon-Ion irradiation.

Methods and Material

The CHO cells were grown on polystyrol-sticks to enable a 2 dimensional view in the headphantom [2]. Cultivation was in DMEM medium supplemented with 10% fetal calv serum and 1% penicillin/streptavidin and kept in a humidified atmosphere of 5% CO_2 at 37° C. Gold nanoparticles of a diameter of 1,9 nm were added to a concentration of 100 µM and incubated for 24 hours. After incubation the cells were fixed on the sticks with methanol at -20°C. Irradiation took place in the NASA Space Radiation Laboratory, Brookhaven with a beam of 2.5 GeV protons. This beam had an estimated range of 10.4 m and an LET of 0.21 keV/µm in water. The size of the beam was about 20 x 20 cm², with an intensity approximately 1,3 Gy/min. After the experiment the sticks were stained for 10 minutes with methylenblue, to prove the presence of cells on the sticks. To investigate the radio sensitizing effect survival curves were made. AG1522D (human foreskin) cells were cultivated in EMEM medium with 1% glutamine, 10% FCS and 1% P/S under standard conditions. Gold nanoparticles of a diameter of 1,9 nm were added to a concentration of 50 µM and incubated for 24 hours. Irradiation was performed with an average LET of 100 and an extended Bragg-peak of 1 cm.

Results

The sticks were irradiated together in a holder perpendicular to the beam direction, with a dose of 100 Gy. The obtained image can be seen in Fig. 1. On the left side is the original image, on the right side the contrast has been enhanced with imageJ software. Analysis indicates an evident enhancement of contrast on the sticks with the gold nanoparticles at an average of 20%.

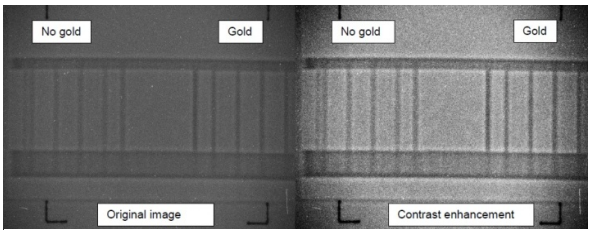

Figure 1: Proton radiography of CHO cells on sticks, with and without incorporated Gold Nanoparticles.

The staining with methyleneblue proofed the existence of cells on the stick, regardless if they contain gold nanoparticles or not, concluding that gold nanoparticles are in fact a possible contrast agent for high energy particle radiation. The experiment also indicates that the protocol of cell treatment leads to the incorporation of gold nanoparticles. The survival curve comparing AG-D cells with and without gold nanoparticle is displayed in Fig. 2. Preliminary results show no increase in radio sensitization for the addition of gold nanoparticles.

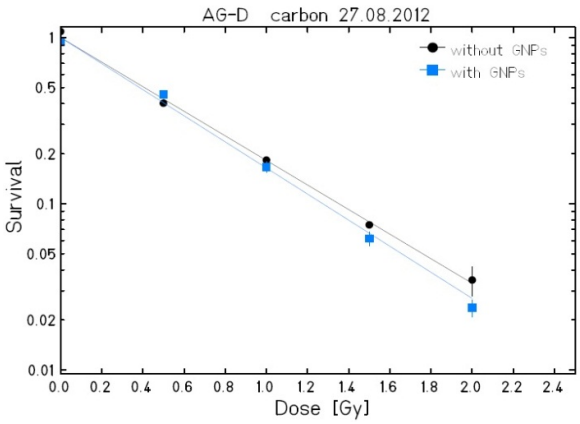

Figure 2: Survival curve of AG-D cells and AG-D cells administered with Gold Nanoparticles

References

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