Heavy Ion Beam Irradiation of a Langendorff Heart

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The Biophysics group at GSI is currently starting experimental studies on radiosurgery of atrial fibrillation (AF) using ^{12}C beams. AF is one of the most common heart diseases. Its prevalence increases with age ($<$ 0.5% in age group below 40, 0.7 % in the age group 55-59 and 17.8% in the age group above 85). In AF, disorganized electrical impulses usually originating in the pulmonary veins cause uncoordinated high frequent (300 - 600 min^{-1}) contractions of the atria (upper heart chambers). Symptoms are low blood pressure, shortness of breath, chest pain, irregular/racing heart beat or extreme fatigue. AF is responsible for 15-20 % of ischemic strokes. A common treatment is the interruption of electric pathways in the heart using catheter ablation. This surgical procedure is challenging, long (about 7 hours), only 52 % of patients can stop medication, 25% are treated at least twice and 6 % suffer from serious complications related to this intervention. A recent study has already demonstrated radiosurgery of the heart in live pigs using photons [1]. Our aim is to reproduce these results while improving target conformity and healthy tissue sparing using ^{12}C. Experiments with pigs and doses in the order of 30 Gy will be performed at GSI in 2014. Similarly to [1], the physiological effect is expected to evolve on the time scale of weeks to months.

The present report describes a pilot study in which we irradiated a small region in explanted pig hearts at HIT Heidelberg with very high doses (up to 160 Gy). The purpose was to gain knowledge about possible acute radiation effects (time scale of hours) resulting from ^{12}C-irradiation. These would be disadvantageous in our pig experiment. In our pilot study we applied dose to the atrioventricular (AV) node as here, a block of electrical conduction can accurately be identified in an ECG trace in real-time.

In each of our three experiments, a heart was extracted from a pig ($\approx$ 30 Kg) and kept in sinus rhythm in a so-called Langendorff setup (cf. Figs 1 and 2) for up to 7 h. The heart was perfused with Krebs-Henseleit (KH) solution via the coronary arteries (flow about 0.5 l/min). Using surgical wire it was fixed in a custom-built PMMA beaker (cf. Fig 2) in a bath of KH. The main circuit of our setup contained about 2 litres of KH. Carbogen gas (95% O_2, 5% CO_2) was used to aerate the solution. About every 30 min., 0.5 l of KH were exchanged to prevent acidfication. The temperature of the KH solution was kept at $T = 37°$C via heated water flowing through a heat exchanger in the oxygenator and the outer volume of the double-walled PMMA beaker. The heart beat induced motion of the myocardium was up to 1 cm. Prior to irradiation, the heart was scanned with 1 mm slice spacing in a PET/CT. The target (AV node) was delineated in the scans. A margin of 1 cm around the target volume (≈ 1.25 cm^3) was added to compensate motion. The initial alignment in the treatment room was performed using room lasers and fiducials attached to the beaker. Orthogonal x-ray images showing titanium clips attached to the heart were finally used to optimize the match with the CT images. Finally, dose was applied in fractions of 5 Gy and 10 Gy over a period of about 3 h. PET and CT scans were made after each experiment.

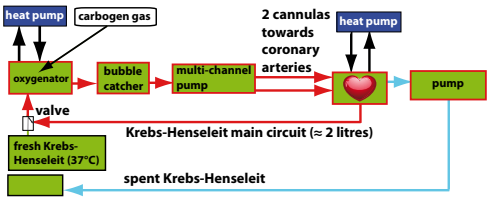

Figure 1: Sketch of the Langendorff setup. The main KH circuit is drawn in red.

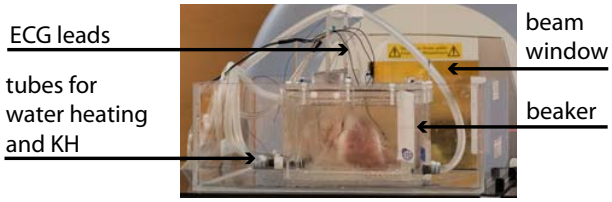

Figure 2: The heart in the double-walled PMMA beaker on the patient couch in the treatment room H1 at HIT. The heart is fixed to the bottom of the beaker with surgical wire.

In our three experiments, we applied a cumulative dose of 80, 90 and 160 Gy to the AV node. Whereas no acute radiation effects could be observed in the first two cases, a block of electrical conduction in the AV node could clearly be identified in the ECG after 160 Gy. On the one hand, this proves that it is possible to influence the electrical conduction system of the heart using ^{12}C beams. On the other hand our pilot study implies that no acute (adverse) radiation effects have to be expected while performing a pig experiment using doses in the order of 30 Gy.

References

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