New Radioactive Implants: First Preclinical Results ◇

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Low dose radiation is known to suppress excessive cell proliferation during wound healing which often limits the clinical success of surgery. Within the RADBIOMAT-Project [1,2] radioactive implants based on polymeric and even degradable materials are developed, produced and tested which use as a radiation source the pure electron emitter ^{32}P. Due to the short electron range of a few millimeters only an integral dose of typically 15 Gy can be administered to the wound region within 7 days avoiding irradiation of sensitive tissue nearby (Brachytherapy). We report on the production of specific implants and first preclinical test on New Zealand white rabbits [3].

Implant production at FZ Karlsruhe

Radioactive implants are fabricated within this project by ^{32}P-implantation. A 180 keV implanter is under construction at the accelerator laboratory for this purpose, in the meantime implants were made using a similar (now closed) facility at the FZ Karlsruhe. ^{32}P was produced by neutron activation at the GKSS nuclear reactor in Geesthacht and accelerated to 60 keV out of an ECR source. A problem for the radiation sensitive polymers was the ^{32}P-beam contamination with ^{31}PH of almost 3 orders of magnitude more intensity. This problem will be solved in our setup by using a sputter source. It has been shown, however, in material tests that ion induced modification of the polymer implants was limited to the 100 nm implantation depth.

Animal tests, ENT clinic

In para-nasal sinus surgery for opening or reopening of a port concluding stenosis can be a major complication. This can be handled in revision surgery by implanting a silicon tube which will be removed after some weeks. However this prevention is not always successful and restenosis is often seen.

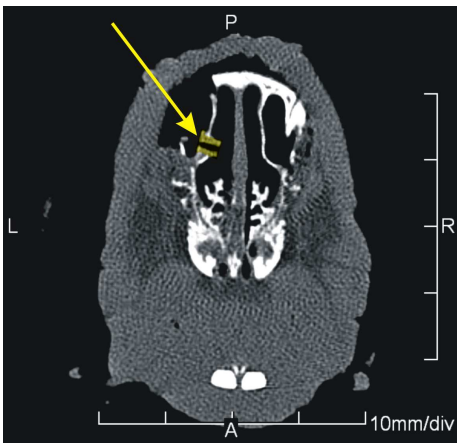

Fig. 1: CT image of a rabbit head with sinus cut and position of the radioactive silicon stent

In order to test low dose irradiation for this case a small silicon stent was developed where ^{32}P was implanted on the outside. This stent was placed for 7 days in the artificially made opening (neoostium) (see Fig. 1). The area of this opening was measured during surgery, after stent removing and 3 month after.

Preliminary result show 52%±25% lumen cross section reduction in the animal group without stents or with non-radiating stents whereas with radioactive stents applying 15 Gy 7-days integral dose almost no reduction (2%±30%) has been found.

Animal tests, eye clinic

Trabeculectomy is the most frequently used glaucoma filtering surgery to lower the intra-ocular pressure (IOP). However it has a failure rate due to fibroblast proliferation of 50% within a year. A small degradable polymer plate (2x2x0.3 mm^3) containing ^{32}P atoms was placed during surgery under a sclera flap to irradiate the surrounding area with an 7-days integral dose of 15 Gy (see Fig. 2). During 5 postoperative weeks the IOP was regularly controlled on both the operated and the unoperated eye. The IOP difference at the beginning typically 6 mmHg is back to 0±1 mmHg after 5 weeks without irradiation, whereas with 5 Gy the IOP difference was found to be 4±2 mmHg and with 15 Gy still at 6±2 mmHg.

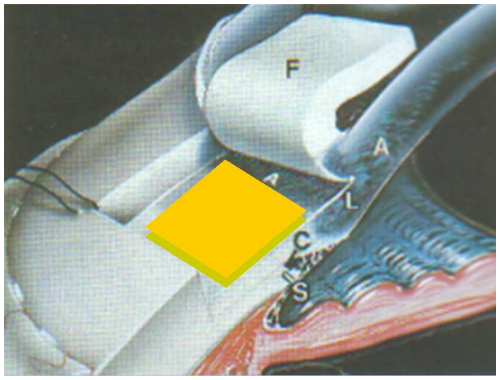

Fig. 2: Schema of trabeculectomie (F: sclera flap) with radioactive implant in position

In conclusion locally administered irradiation at a very low dose rate can prevent restenosis or scaring in animal tests with significant statistic and could avoid anti-metabolites such as mitomycin C in critical situations.

References

[1] W. Assmann *et al.*, Annual report 2003, p. 67-68
[2] M. Schubert *et al.*, Annual report 2004, p. 65-66
[3] W. Assmann *et al.*, Int. Conf. of Medical Physics (ICMP2005), Nürnberg (Sept 2005)

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