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A bile flow model for in-vitro testing of biliary stents – a prognosis of incrustation processes

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The endoscopic insertion of plastic biliary endoprostheses is an effective and well−established treatment for biliary strictures. Plastic stents are easy to insert and to remove. In comparison to the competitive self-expandable metallic stent plastic stents are also cost-saving. The major limitation of this technique is the short patency period, which can vary between only weeks to a few months.
There have been several efforts to prolong the patency period of biliary plastic stents. Some attemps have shown promising results during the in-vitro testing but so far none of the results could be confirmed by following in-vivo studies. The discrepancy between the tests results of in-vitro and in-vivo studies might be due to inadequate in-vivo models.
To tests newly developed biliary stents under conditions close to physiological ones a bile-flow model has been developed, which not only considered the physiological temperature, position and pressure of the bile duct but also the discontinuous volume flow of bile. Above all, the set-up provides the opportunity to measure the volume flow through the stent. This innovation leads to the possibility to observe how the volume flow decreases over time by occurring incrustration and to determine the time of stent occlusion.
The model is designed to pump bile (porcine or human) from a heated reservoir to higher situated reservoir. The fluid flowes through several connected stents by the force of gravity. A constant hydrostatic head ensures a pressure close to the physical one. For each stent the volume flow is measured separatly and contactless by a drop counter. The flow rate can be regulated by a steplessly adjustable tube clamp.
Aim of the bile flow model is to be more authentic and therefore to enable reliable prognosis concerning patency periods of new stents. In-vitro findings made with this model claim to be easier transferred in later in-vivo testing results.

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Optimisation and validation of an FEA model for the simulation of the electrical flow through fish heads

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The aim of the study was to validate and improve a computer model to simulate electrical current through a fish head using the finite element analysis (FEA). The specific conductivities for the tissues and organs used in the model were taken from the literature. Since these are data for human tissue, there are presumably significant deviations to the actual conductivities of the fish. Two fresh fish heads from a slaughter were used to validate the model. Under X-ray control a tip of a cannula was placed centrally in the brain of the fish head. The cannula was isolated except for the tip (2 mm). The second electrode (surface electrode) was a screw (radius 1.5 mm), which was placed at different locations on the surface of the head. The applied AC voltage had a value of 11.45 V. The currents between the electrodes were measured. The FEA model was extended by the additional electrodes. The original ambient material (water) was replaced by air. The current between the brain electrode and the respective surface electrode was determined by integrating the current density over the brain surface. The comparison between the experimental and the calculated current densities showed large deviations when the surface electrodes had skin contact. Therefore, the conductivity of the skin was varied. In order to determine the optimum conductivity, the measured and calculated currents were set in relation to the current intensity, which was determined between the eye electrode and the brain electrode, since no currents flowed through the skin. The optimum conductivity of the fish skin was assumed if the ratios of the experimental sites corresponded to the theoretical current ratios as well as possible. When the optimized conductivity was used, all the calculated and experimental current ratios were in good agreement.

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Influence of total tumour volume on BED values – simulation study using a PBPK model for ^{177}Lu-labelled PSMA ligands

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Advanced prostate carcinoma can be treated using prostate specific membrane antigen (PSMA) labelled with ^{177}Lu. The amount of injected peptide influences the biologically effective doses (BEDs). The influence of the unknown total tumour volume on the BED values of the tumour lesion and the relevant organs was not yet investigated. Therefore, the aim of this study was to investigate the influence of tumour volume on the BED values of the accumulating organs, i.e. two tumour lesions, the rest tumour, the salivary glands and the kidneys.
Eight patients with metastasized prostate cancer received an average activity of (7.2±0.34) GBq ^{177}Lu-labeled PSMA-specific peptides of (87.7±4.1) nmol. A physiologically-based pharmacokinetic (PBPK) model was used to simulate the biokinetics and resulting BEDs of each patient for an assumed total tumour volume between (0.1-10) l, the BED values of the rest tumour, 2 tumour lesions and organs at risk were calculated.
The average BED values of these patients for lesions, kidneys and salivary glands were (22.7±13.1) Gy, (5.7±2.2) $Gy_{2.5}$ and (13.9±5.2) $Gy_{7.5}$, respectively. Relative to tumour volumes of 0.1 l, for tumour volumes of 0.3, 1, 3 and 10 l, the lesion BED values decrease to (95±3)%, (83±10)%, (63±17)% and (36±18)%, respectively. For kidneys the decrease is (95±4)%, (83±11)%, (62±18)% and (36±17)%, and for salivary glands it is (95±3)%, (83±11)%, (62±17)% and (35±17)%.
BED values of the tumour and other relevant organs depend on the tumour volume in all patients differently. Therefore, for individualized optimization it is important to find an accurate calculation method for the total tumour volume to determine correctly the optimal amount of peptide and activity for each patient.

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Development of an algorithm for selecting the optimal radiopharmaceutical to molecular radiotherapy

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Peptide Receptor Radionuclide Therapy (PRRT) is increasingly used for treating neuroendocrine tumors (NETs). Kidneys and red marrow are usually the limiting organ at risk for PRRT. Kletting et al. recently developed an approach for obtaining an improved therapeutic result based on the estimation of the optimal combination of amount and activity for PRRT. In this work we aim at developing an approach to predict the optimum biodistribution based on the optimal combination of the type of radionuclide and peptide affinity. Therefore, a PBPK model for ^{111}In-DOTATATE developed in Matlab Simulink (R2017a) by Kletting et al. was adopted. Individual physiological parameters were taken from an average of 5 patients with NET. The parameters representing radionuclide half-life (decay constant) and peptide affinity (dissociation constant K_D) were varied with a fixed dissociation rate k_{off} value of $0.04s^{-1}$. A starting minimum half-life of 1h was used and incremented by powers of two upto 128h and adding 64.1h (^{90}Y), 161.5h (^{177}Lu) and 194.3h (^{131}I). The K_D starting from 0.1 nmol/l was incremented by powers of two upto 102.4 nmol/l. The peptide amount was fixed to 4 nmol with an infusion duration of 60 min. The therapeutic index (TI) was calculated as the ratio of the time integrated activity coefficients (TIACs) in the tumor to the TIACs in the organs at risk (OAR), i.e. kidney, red marrow, liver and spleen.
For kidney, liver and spleen, the optimal TI was obtained for a combination of a radionuclide with a short half-life (1-4 h) and a peptide with a large K_D value (102.4 nmol/l). However, for red marrow the optimal TI value was obtained for a combination of a long half-life (194.3 h) and a low K_D value (0.1 nmol/l). Hence, the physician has to take into account the trade-off between different OARs before making an individualized decision.

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Dynamic 7 layer model to generate synthetic signals for non-invasive fetal photoplethysmography

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Non-invasive fetal photoplethysmography is a method to capture the fetal pulse using optical absorption characteristics of pulsing arteries. A light source and photodetector are placed on the abdomen of the pregnant woman. The acquired signal carries information of the fetal heart rate and may be potentially used to compute the fetal oxygen saturation non-invasively.
The properties of the mixed fetal and maternal signal measured with this setup are widely unknown. Amplitude, kind of signal coupling and further information about the light source and photodetector need to be investigated. The starting point for further research is the dynamic 7 layer tissue model, described in this work.
The model consists of 7 slices representing several maternal and fetal tissues and arteries. In contrast to former presented tissue models, the diameter of the fetal and maternal arteries are time dependent. Light propagation is modeled using the helmholz equation interface of COMSOL Multiphysics. Reflections on tissue boundaries are taken into account by applying Robin-type boundary condition. The time varying model allows to set parameters like sampling rate, diameter of the fetal and maternal arteries and the position and number of light sources and photodetectors.
With the results of the simulation it is possible to analyse deterministic synthetically generated signals in time and frequency domain. These synthetic datasets will be used as a ground truth, since clinically measured signals are not available and difficult to analyse due to their highly stochastic character. The signals allow us to benchmark and optimize algorithms developed to extract the fetal and maternal pulse curve from the acquired signal mixture. Further, the simulations are a usefull tool to analyse source-detector configurations and to confirm the feasibility of non-invasive fetal photoplethysmographie and pulseoximetry.

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Comparison of different Monte-Carlo-simulation software for phantom study in fluoroscopy

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One interesting development in radiology is the use of Monte-Carlo-based simulations in comparison to real measurements. Especially in education of engineers the knowledge of advantages and disadvantages of different simulation software could be very useful for future work. So, we want to develop an experimental design for master students in Biomedical Engineering for area dosimetry and the verification with Monte-Carlo-based simulations.
Practical measurements took place in one of our X-Ray-laboratories. There is an X-Ray-tube for fluoroscopy with image intensifier. Different ionisation chambers were used for area dosimetry while fluoroscopy of a 10-cm thick water phantom with 100kV and 10x10 cm²-field. Values were taken from different positions in radiation field, especially for scattering besides and diagonally behind the phantom. Additionally, the dose values were taken in different heights, for example for estimation of eye lens dose.
In a second step the real measurements were simulated with different Monte-Carlo-based systems. There are a lot of systems on the market. We started with FLUKA from CERN. In comparison to these results we used EGSnrc from National Research Council Canada as a second system. Simulations with Penelope from Nuclear Energy Agency are still in progress.
The spectral distribution of X-Ray-tube was modelled by information from manufacturer. In all simulations, we varied the number of photons between 500.000 and 5.000.000.
Results of FLUKA and EGSnrc are quite similar. Differences to the measured dose values were observed. An actual master thesis investigates the causes for the differences and the usability of Monte-Carlo-simulation in education of master students.

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3D-Modell der Tuba Eustachii aus Fusionierung histologischer Schnitte und des CBCTs – Grundlagen funktioneller Aspekte

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Einleitung: Bis heute ist der exakte biomechanische Ventilmechanismus der Tuba Eustachii (TE) nicht hinreichend aufgedeckt. Dysfunktionen der TE stellen bis heute eine medizinisch relevante Pathogenese dar. Interventionelle Ansätze direkt an der TE werden seit langem immer wieder versucht, sind bislang aber nicht in der gewünschten Zuverlässigkeit wirksam. Eine 3D-Modellerstellung bietet u.a. die Möglichkeit, das Verständnis für regelhafte Tubenfunktion bzw. Dysfunktion zu vertiefen und ggf. neue physikalische Therapieverfahren zu simulieren.
Methoden: Das 3D-Modell wurde erstellt aus der Fusion eines CBCT eines markierten und eingebetteten Gewebeblocks einer Tuba Eustachii eines Schwarzkopfschafes sowie der anschließen angefertigten digitalisierter und segmentierter histologischer Schnitte.
Ergebnisse: Der 3D-DICOM-Datensatz des Gewebeblockes des CBCTs und die digitalisierten histologischen Schnitte konnte anhand Markern zu einem konsistentem 3D-Volumen fusioniert werden. Eine quantitative Auswertung und Relation ist nach Segmentierung der Kompartimente (Knochen, Knorpel, Muskel, Mucosa, Submukosa) möglich.
Schlußfolgerungen: Mit Etablierung dieser Methode ist einerseits eine hochaufgelöste und quantitativ exakte anatomische Topographie verfügbar. Zudem kann diese 3D-Modellbildung Grundlage für weitere funktionelle Studien sein, welche ein tieferes Verständnis der vermutlich hydraulischen Ventilfunktion geben und für die Entwicklung individualisierter Stentsysteme maßgeblich sein.