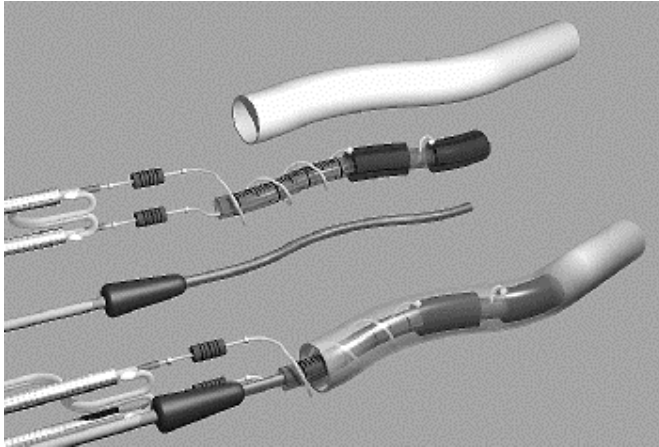


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The framework

Using heat for the treatment of malignant tumours is becoming standard treatment. However, it has proven to be far from easy to produce controlled temperature distributions in living tissue. The development of elaborate diagnostic scanning systems and the availability of considerable computational power has opened the way to direct physical modeling of the absorbed power distribution and temperature field in the tissue of the patient.

The work described in this thesis was focused on the preparation of the clinical introduction of a specific interstitial hyperthermia system, the Multi-Electrode Current Source Interstitial HyperThermia (MECS-IHT) system. In order to be able to plan a treatment with this system, and also to investigate the physical properties of the proposed treatment method, a number of computer models have been designed, implemented and tested and special procedures for the simulation of actual treatments were devised.

The MECS-IHT system.



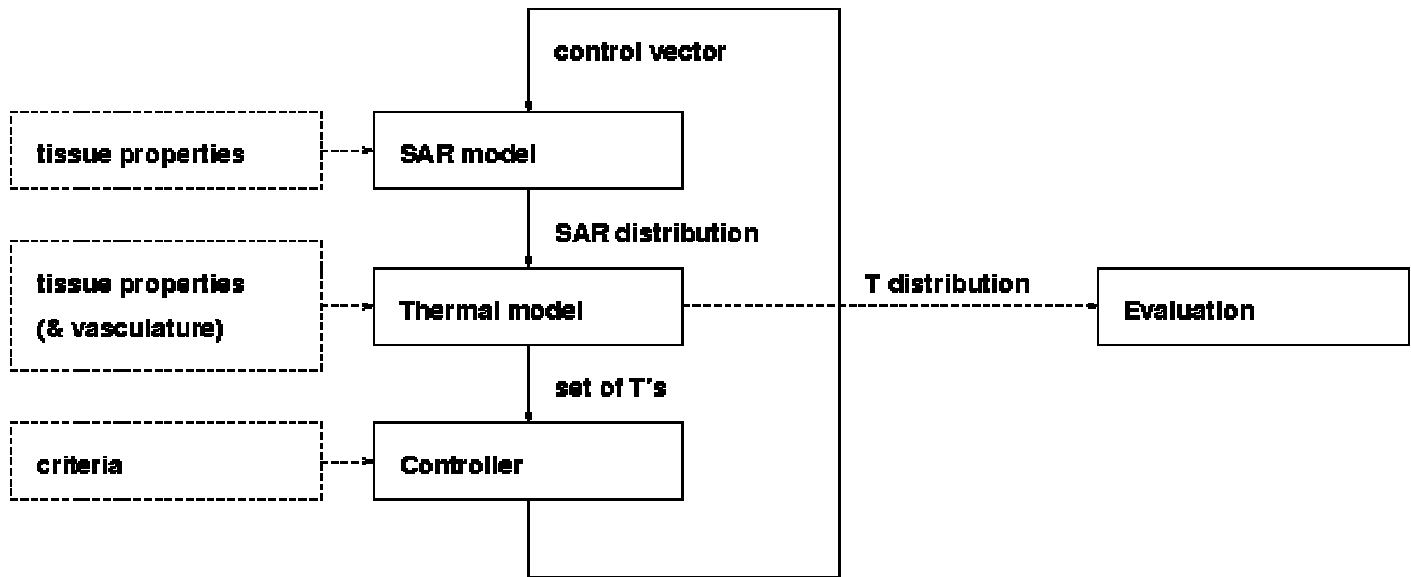
The main physical problem of local hyperthermia is the strong spatial variation of the removal of heat from the treatment volume by blood flow.

Local hyperthermia systems work by administering heat to the target volume and its immediate surroundings. In order to create an acceptable temperature distribution in the target volume the spatial distribution of the heat deposition must be adapted to the heat removal pattern in the tissue.

In 1991, Lagendijk and Visser started the development of a new capacitively coupled interstitial hyperthermia system, addressing this fundamental problem in local hyperthermia technique. The system devised consists of numerous metallic electrodes connected to high-frequency power sources, inserted in plastic catheters. The coupling between the power sources and the tissue is dominated by the capacity between the tissue and the electrode: the dielectric catheter wall. Thus, relative independence of the electrical properties of the surrounding tissue was attained. It proved to be possible to place several independent electrodes in a single catheter. In this way, the heat deposition along the catheter track can be adjusted, allowing finer spatial SAR control than previously available.

A very strong point of the MECS system is that it incorporates extensive thermometry in the target volume. The temperature data acquired in the applicators can be used for real time feedback control of the power deposition of the system.

The planning system



In a given patient situation a number of choices must be made to determine the parameters of the treatment. For example, the placement of the heat sources and their relative phases must be defined.

The process of selecting optimal parameters for the treatment is called treatment planning. The input for the planning procedure is a set of data concerning the patient: volume scans of the affected tissue and surroundings, vascular structures in and near the target volume, the target volume definition, geometrical constraints, etc.

The results of the planning should be a recipe for the implantation of the catheters and the electrode configuration and detailed information on the temperature distribution which can be expected.

The treatment planning is implemented as an iterative process. Once a certain choice is made for the treatment parameters, physical models of the heating system and the heat transport in the implant are used to assess the given setup. If the assessment of the setup is unfavourable, certain parameters can be changed (mostly 'by hand') and the assessment procedure is restarted. Parameters of the setup *can* be changed automatically in the treatment planning system, most notably the intensity of the heat sources. This opens the way to a realistic simulation of the dynamics of the treatment system.

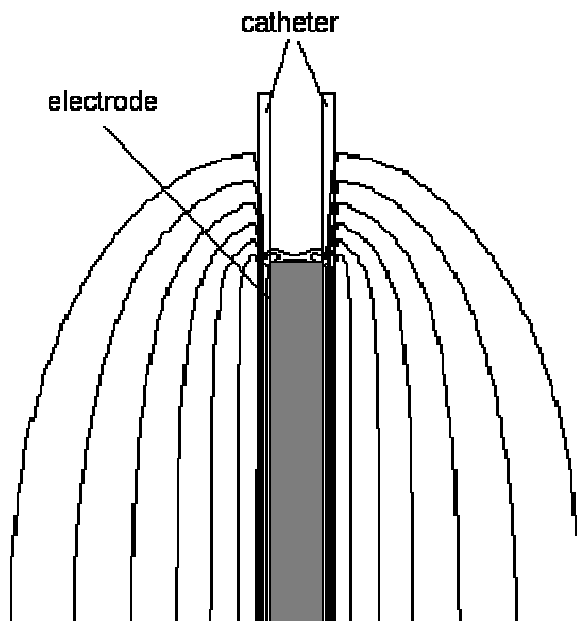
Once a treatment is set up in a patient, reconstruction of the actual relative position of the relevant structures should be used for further treatment simulation.

The treatment planning system developed in the Utrecht research group consists of a number of modules:

- calculation of the power deposition in tissue;
- thermal model incorporating discrete vasculature;
- feedback controller used to optimise electrode settings;
- software for analysing temperature distributions;
- vessel reconstruction software;
- implant planning software;
- visualisation of the temperature distributions in tissue and along vasculature;
- visualisation of the implant setup.

A use of the planning system that is not directly of benefit for a specific patient is the investigation of general physical properties of the heating technique. In this way, the planning system is used to gain better understanding of the interaction between the treatment (power deposition) system and the patient (heat transport) system.

The electrical properties of the applicator

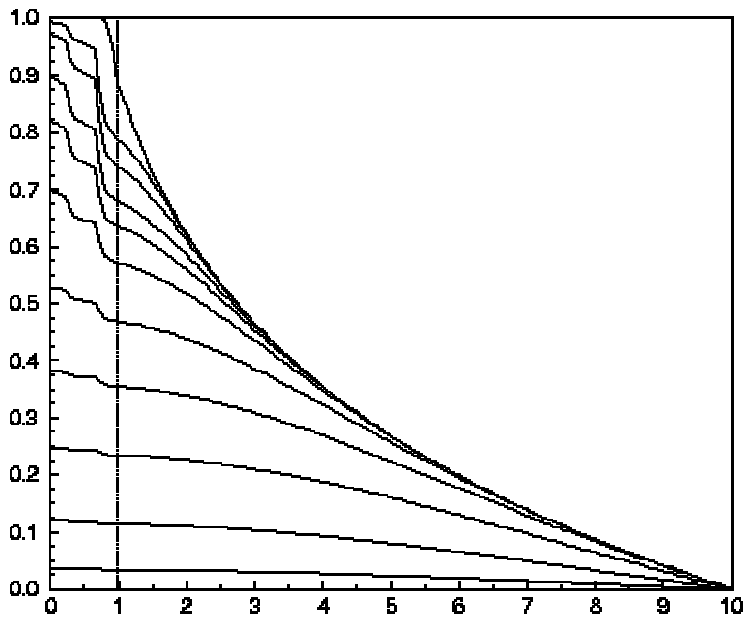


Multi electrode current source interstitial hyperthermia (MECS-IHT) employs individually controlled, 27 MHz radiofrequency electrodes inserted into plastic brachytherapy catheters.

In order to get a firm understanding of the physical behaviour of the electrodes and to verify the current source approximation in the hyperthermia treatment planning system we have investigated (1) the electrical properties of the electrode-catheter-tissue system and (2) the impact of inhomogeneity of the electrical properties of the tissue in the vicinity of the electrodes.

The results validate the use of the ideal current source approximation in the treatment planning SAR model. The models predict the presence of a significant heat source inside the electrode wall when lossy catheter materials are used, producing a conductive heating component in addition to the SAR in the tissue. For a given catheter spacing this conductive component will produce a more heterogeneous temperature distribution. Thus, the use of low-loss catheter materials like polyethylene and Teflon is recommended. In case of efficiency problems with the treatment system a compromise can be struck between a more lossy wall material and a less good penetration depth of the heating.

The thermal properties of the applicator

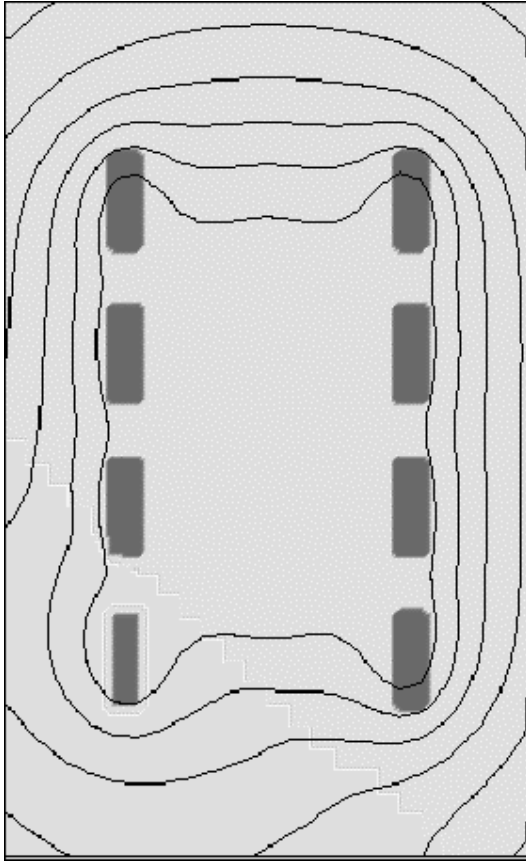


The thermal influence of self-heating of the catheter was investigated and an analysis of the measurement of temperatures inside the catheter during and after heating was made. Analytical models and a high resolution numerical model were used for the calculation of steady state and transient distributions, respectively. The model results were compared with experimental data obtained in a muscle equivalent phantom. The results from these investigations indicate that there is no significant difference between the temperature inside or outside the catheter when using low-loss catheter materials. Self heating in the catheter wall has an adverse effect on the uniformity of the stationary temperature distribution and the reliability of temperature measurement with the internal thermometry. This effect remains within acceptable limits for mildly lossy materials, where there is only a 6% difference between the temperature increase inside and outside when using low-loss Nylon.

Distortion of temperature gradients measured along the catheter was also investigated. Key factors are the thermal conduction across the thermocouple wires and especially the presence of minute layers of air between consecutive layers of the probe. The distortion extends less than two millimeters, which is acceptable.

The simulation results are compatible with measurements in phantoms and show that, if the proper choice of materials is made, the MECS applicator answers to our expectations and that the temperature measurement inside the catheter can be used for direct feedback treatment control.

Anatomical models without discrete vessels



The quality of temperature distributions that can be produced with the MECS-IHT system was investigated using computer models of idealised anatomies. These much idealised anatomical models did not contain discrete vessels. Binary media anatomies, containing media interfaces oriented parallel, perpendicular or oblique with respect to the long axis of the implant represented simple anatomies which *can* be encountered in clinic.

A 7 catheter hexagonal implant geometry with a nearest neighbour distance of 15 mm was used for the investigations. In each interstitial probe between 1 and 4 electrodes with a diameter of 2.1 mm were placed along an 'active section' with a length of 50 mm.

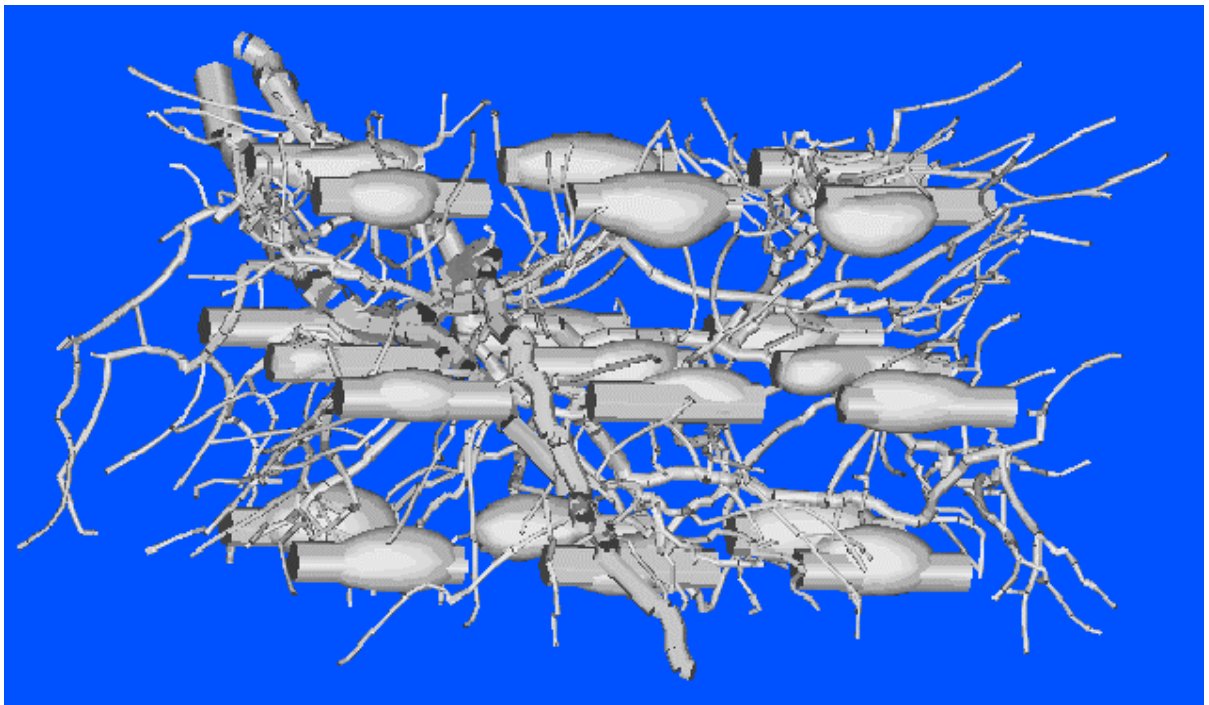
The study showed that even with high contrasts in electrical and thermal conductivity in the implant it remains possible to obtain satisfactory temperature distributions with the MECS system. Due to the 3D spatial control the temperature homogeneity in the implant can be made quite satisfactory, with $T_{10}-T_{90}$ in the order of 2-3 K and a maximum temperature rise of 7 K in the volume. It is important to emphasise that treatment planning must ensure that the placement of the current source electrodes is compatible with the media configuration.

The minimum sensible length of the individual controllable electrodes is in the order of the catheter spacing. Using shorter electrodes does not notably improve the temperature distributions in well-positioned implants. Temperature control improves dramatically when going from a single to two segments; further segmentation has less effect. To further improve the temperature distributions the spacing between the

catheters, 15 mm in the simulations, may be decreased, which would improve the lateral SAR control.

Inhomogeneities present in the implant volume lead to inferior temperature distributions if no longitudinal SAR control is available: it is then impossible to devise an electrode configuration compatible with the anatomy. If there is a limited amount of spatial control and the inhomogeneities are of comparable or larger scale, careful planning of the geometrical electrode configuration is essential. The performance of electrodes extending through the interface between media can be compromised. Although the effects seen in the CTVH's in these cases may not be spectacular, there can be significant local deviations from the prescribed temperature, which may have serious consequences for tumour control.

Anatomical models with discrete vessels



Simulations including the effect of simple large vessel structures and complex vascular networks (both homogeneous and heterogeneous perfusion) demonstrate the great effect of blood flow on the temperature distributions obtained. The spatial SAR control of the MECS IHT system, combined with the temperature feedback available, is essential for optimizing the temperature uniformity.

Even if over-dosage in large parts of the tumour is acceptable the spatial control is needed to avoid overheating of the normal tissue in or near the target volume and to make the thermal dose distributions controllable by the clinician. The optimal length of the electrodes is in the order of the catheter spacing. The use of shorter electrodes does not notably improve the temperature homogeneity.

Further research is needed to investigate the parameters which are important for optimal temperature control in patients treated with the MECS IHT system; the parameters of interest include location, spacing, length and phase of RF electrodes in relation to the locations of large vessels, clusters of large vessels (high vessel density),

the dielectric anatomy and the effective thermal conductivity anatomy. Current research is aimed at obtaining practical clinical guidelines for optimal system settings in individual patients.

Epilogue

The clinical introduction of the MECS-IHT system is now well on its way. In Rotterdam, Utrecht and Amsterdam treatment protocols have been designed which are aimed at treating brain tumours, the prostate and soft-tissues. Present actual treatments with the system are technically successful.

Patient specific treatment planning in hyperthermia is still immature, mainly due to technical problems in the field of data acquisition (vessel reconstructions, dielectric and thermal tissue properties). *In-vivo* and phantom tests of the treatment planning system are currently running. These items are subject of a new project funded by the Dutch Cancer Society (NKB). The planning system, and notably the thermal model, developed during the project has proven to be versatile and powerful. For the first time, it has allowed us to faithfully model the detailed thermal behaviour of complex and realistic vessel networks.

The further development of the planning system and the MECS-IHT system towards full clinical usability is a formidable challenge. A concrete foundation is present. This research was supported by the Dutch Cancer Society and Nucletron International.

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