Numerical modelling of heat transfer in hyperthermia

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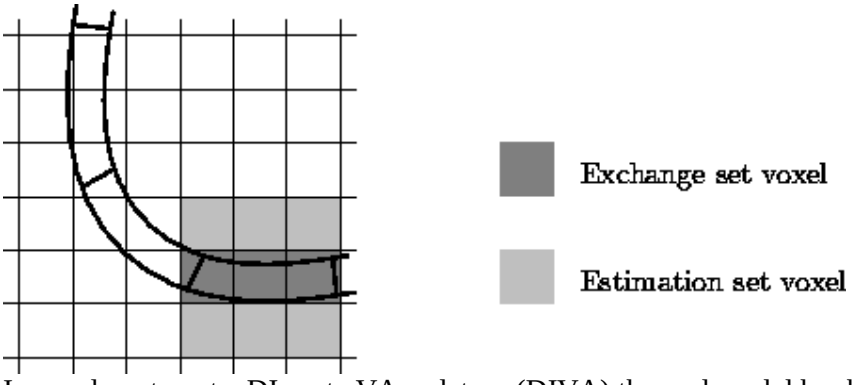
Summary

Hyperthermia treatment is the induction of temperatures above 41°C in order to treat disease. The clinical application of hyperthermia is mainly as an adjuvant therapy to radiotherapy and/or chemotherapy against cancer. One can distinguish between three types of hyperthermia: local, regional and whole-body. In local hyperthermia, heating is limited to the tumour and a small margin of the surrounding healthy tissue. Because the temperatures in the rest of the body remain (nearly) normal, the blood that supplies the tumour will be relatively cold. Tissue in the treatment volume that is close to an artery may as a result remain below the desired treatment temperature. The problems in reaching therapeutic temperatures in all of the treatment volume are hindering the use of hyperthermia in the clinic.

One strategy for preventing regions of thermal underdosage is by compensation through power steering. More heat must be deposited where there is localised cooling caused by the larger vessels. For this strategy to work, the power deposition must be controlled three-dimensionally on a centimetre scale. To use the power steering to optimum effect, treatment planning is necessary, as well as sufficient feedback on the temperature distribution during treatment. The thermal model to be used in treatment planning, monitoring, and evaluation must account for each of the large blood vessels individually. Three-dimensional imaging techniques can give information on the vasculature for use in a discrete vessel thermal model, but at present it is not possible to recover all thermally significant vessels. Therefore, part of the true patient vasculature must be modelled in an alternative way.

Figure 1: In the DIVA thermal model, vessels are described as geometrical objects, separate from the 3-D tissue grid. Thermal interaction is dealt with through the use of "estimation" and "exchange" voxels. The figure shows a vessel segment, divided in several so-called buckets, which are the elementary parts of the vasculature in the model.



In our department a DIscrete VAsculature (DIVA) thermal model has been developed which elegantly handles branching and curving vessels. In the calculation of the heat exchange between a vessel and the surrounding tissue, this model makes a number of

assumptions. The assumptions allow the model to handle detailed vessel networks without requiring an excessive amount of computer memory. When this model was presented, it was shown that for situations conforming to these assumptions there was excellent agreement between the results of the model and theoretical predictions. In the first two chapters of this thesis, the accuracy of the thermal model is investigated for situations where not all of the assumptions are valid. In Chapter 2 it was shown that for large voxel sizes with respect to the voxel diameter the accuracy of the calculated heat exchange was still good to excellent. However, the freedom that the model offers to position the blood vessels anywhere with respect to the voxel grid was shown to be a factor that could deteriorate the accuracy of the calculated heat transfer. In Chapter 2 it was furthermore demonstrated that curved vessels can be accurately modelled, provided that the voxel size is not very small with respect to the curvature of the vessel. In Chapter 3 the accuracy of the model for counter-current vessels was investigated. The presence of a second vessel in the direct vicinity of a blood vessel indirectly violates one of the assumptions in the calculation of the heat transfer between vessel and tissue: the temperature distribution will no longer be cylindrically symmetric around the vessel. This particular choice to test the applicability of the model for non cylindrically symmetric situations was made because of the frequent occurrence and suggested important role of counter-current vessels in the thermal behaviour of vascularised tissue. It was demonstrated that the accuracy of the model is very much dependent on the resolution used in the computations. For voxel dimensions smaller than the diameter of the modelled vessels the error in the simulated heat exchange was found to be a few percent or less, except for very small distances between the vessels. For larger voxel sizes the accuracy is not simply less, it is also more dependent on the exact model geometry. The model geometry does not only consist of the vessel configuration, but also of the position and orientation of the vessels with respect to the discretisation grid.

Figure 2: Artificial vessel describing a helix. This geometry was in Chapter 2 used to investigate the accuracy of the model for curved vessels.

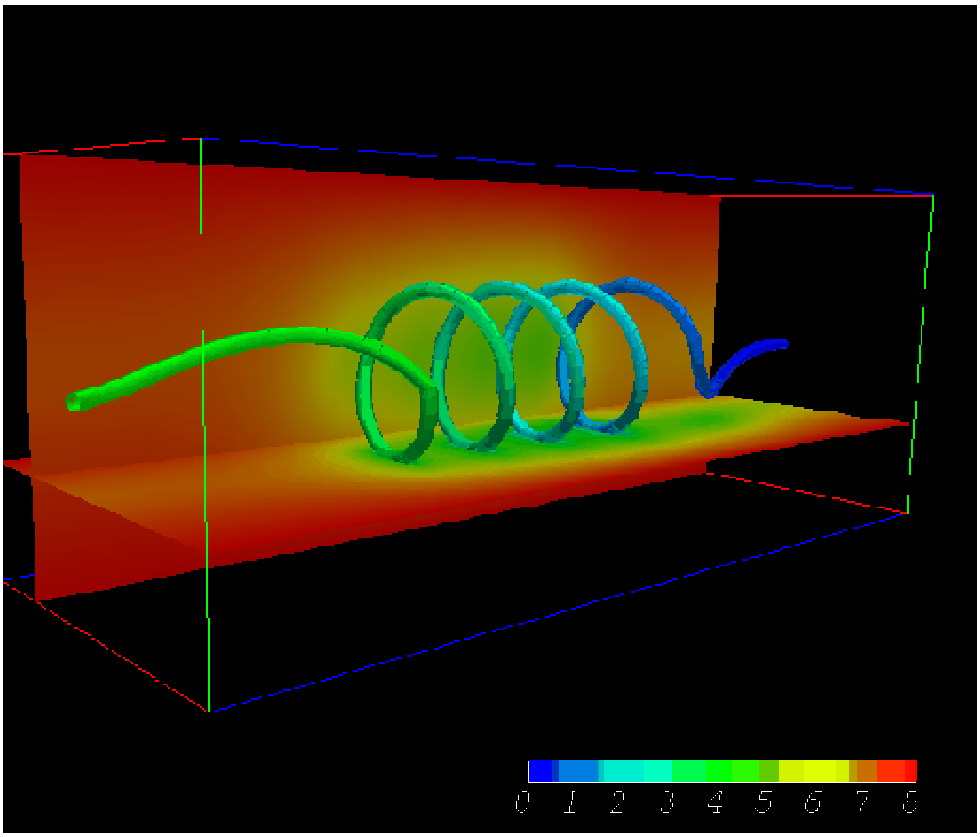
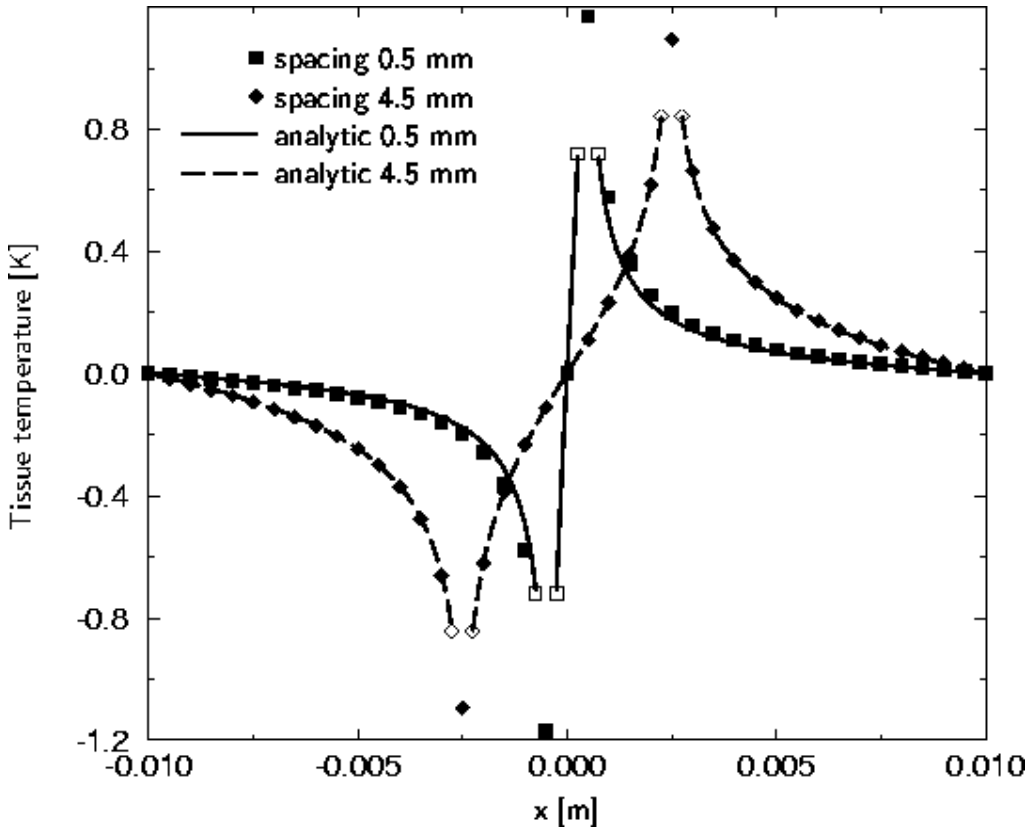


Figure 3: Temperature profile on line through two counter current vessels in a tissue cylinder. The wall temperatures according to the program are indicated by open symbols. There is very good agreement between model prediction and analytical results.



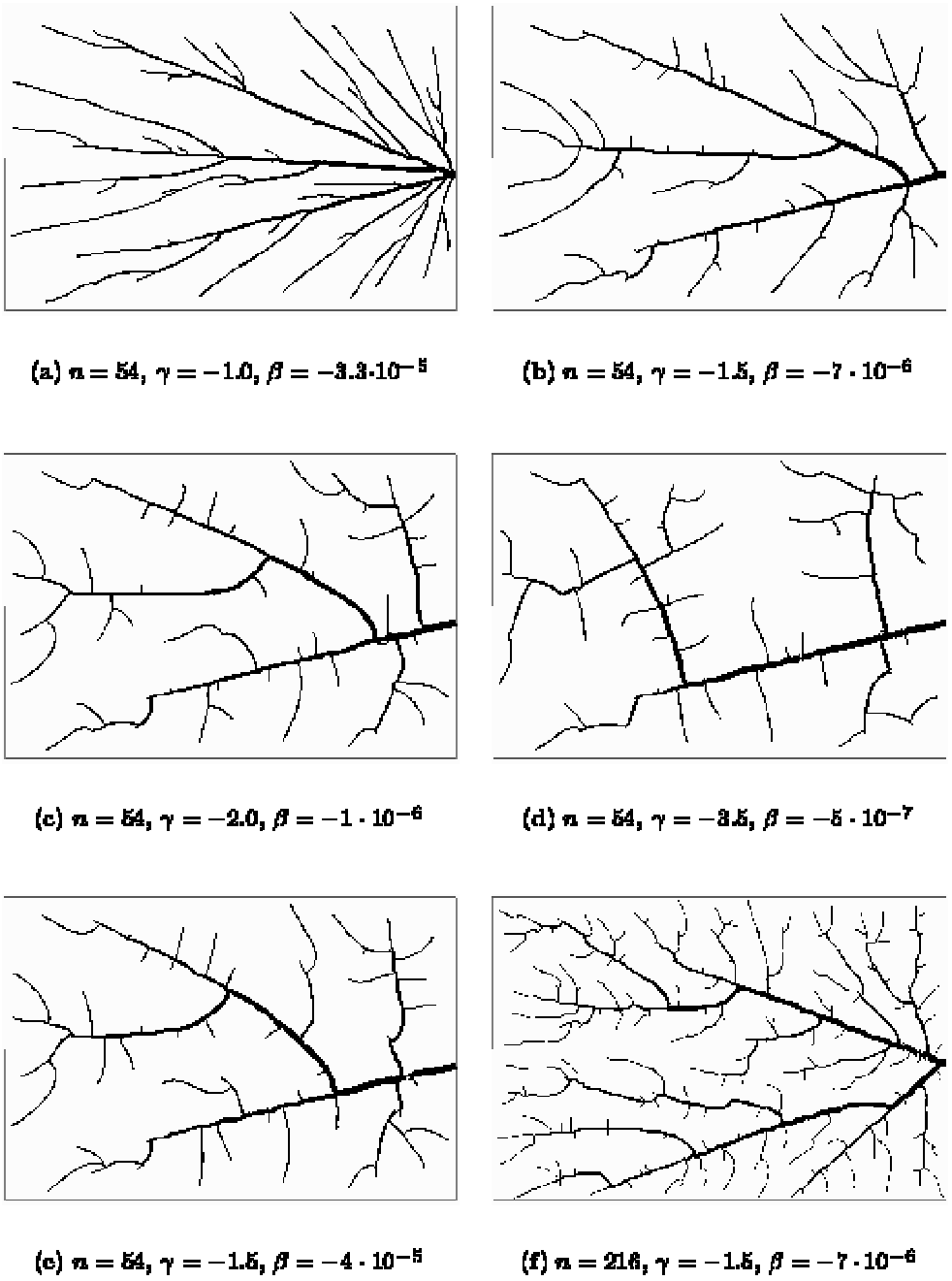
In the evaluation of predictions made by the model, it must be realised that the inaccuracies introduced by the model in the description of the discrete vessels are often not the only ones. In the clinic many relevant parameters are not precisely known and/or may change during hyperthermia treatment. An example is the possible increase in blood supply as a reaction to the rise in temperature. The limited accuracy of the parameters will often seriously limit the achievable precision of the model predictions. Increasing the resolution of a simulation, at the cost of calculation time, will be of little use as soon as highly inaccurate or incomplete input data sets are the dominant source of errors.

The discrete vessel thermal model enables numerical study on the problem of how to model that part of the patient vasculature that is practically invisible to present day imaging techniques (ø < 1mm). The applicability of alternative (continuum) formulations can be compared against the numerical solution obtained with individual vessels. Two alterations to the continuum heat transfer equation have been most popular to describe the effects of blood flow. The first is the addition of a heatsink term describing the thermal equilibration of arterial blood to the local tissue temperature. The second is an increase in the thermal conductivity coefficient, describing the convective heat transport by pairs of vessels that are in near thermal equilibrium with the surrounding tissue. Theoretical considerations have

demonstrated that qualitatively the influence of large vessels is appropriately described by a heatsink term, whereas for small vessels the effective conductivity description is suited. In between there is a range for which neither of the models is very accurate.

In Chapter 4 the applicability of the effective conductivity description for comparatively large vessels is tested in simple geometries. Previous theoretical results for a single counter-current vessel pair, in which the three-dimensional problem was reduced to three coupled one-dimensional equations, were demonstrated to give a small overestimation of the counter-current equilibration length. The discrete vessel simulations affirmed that an effective conductivity can be attributed to counter-current vessels and that the effective conductivity description becomes increasingly inaccurate for larger vessels. The latter result is related to the fact that for larger flow a larger length is necessary for the radial temperature distribution to develop. If the actual length of the problem is short compared to this length, the vessel pair will primarily behave as a heatsink. Straight vessel pairs were also used to build a highly regular, non-branching vessel network. The temperature distribution around a large blood vessel passing through this simple network was calculated. This was also done after removing the small vessels and increasing the thermal conductivity. It was found that in this geometry the thermal effect of the small vessels could not be modelled satisfactorily by an enhanced conductivity. This was the case even if the blood velocity in the small vessels was small. Specifically, the temperatures in the bulk of the tissue corresponded to a higher effective conductivity than was compatible with the long thermal equilibration length of the large vessel. In other words, the radial temperature gradient close to the vessel is larger than might be expected on the basis of the more distant tissue gradients.

Figure 4: Vessel networks in thin tissue slice constructed with VAMP using different parameter sets. Parameters γ and β influence the construction process, *n* is the number of terminal vessels. In networks (a) to (e) the same set of end points was used.



To study the thermal behaviour of real branching vessel networks, detailed three-dimensional vessel networks are needed. Because sufficiently detailed descriptions of real vessel networks are not readily available, the need for a computer program that can construct realistic vessel networks was felt. In Chapter 5 a new program for the construction of vessel networks was presented. This program, VAMP (Vasculature Assembly through Modifiable Potential), can elegantly account for different

perfusions in different tissues. Although the model does not try to emulate real angiogenetic vessel growing processes, the technique to produce connected vessel networks was shown to be capable of producing physiologically realistic networks. Because it is possible to use vessel networks as input, the algorithm can also be used to add detail to real but undetailed vasculatures.

Using a VAMP-generated vasculature, the thermal behaviour of vascularised tissue was studied in Chapter 6. In the first place the ability of the DIVA thermal model to do numerical studies that include the vast majority of the thermally significant vessels was demonstrated. For the partially heated tissue volume and low perfusion values it was found that considerable heat exchange took place in the large arteries of the arterial network. Although the network modelled homogeneous perfusion, this resulted in an inhomogeneous cooling field. Because of this, an incomplete discrete description of the vessel network provided a better prediction of the temperature distribution than is obtained using the heatsink equation, even though the thermal description of the removed small vessels leaves room for improvement. The validity of combining crude vessel networks with an enhanced thermal conductivity to model the effect of the smaller vessels is still unclear. To study this, a change in the thermal model is necessary.

Figure 5: Temperature isosurface for temperature rise of 4 K in a heated tissue cube, in which a detailed artificial vasculature is present. The legend describes the color coding of the vessel blood tempertures in K.

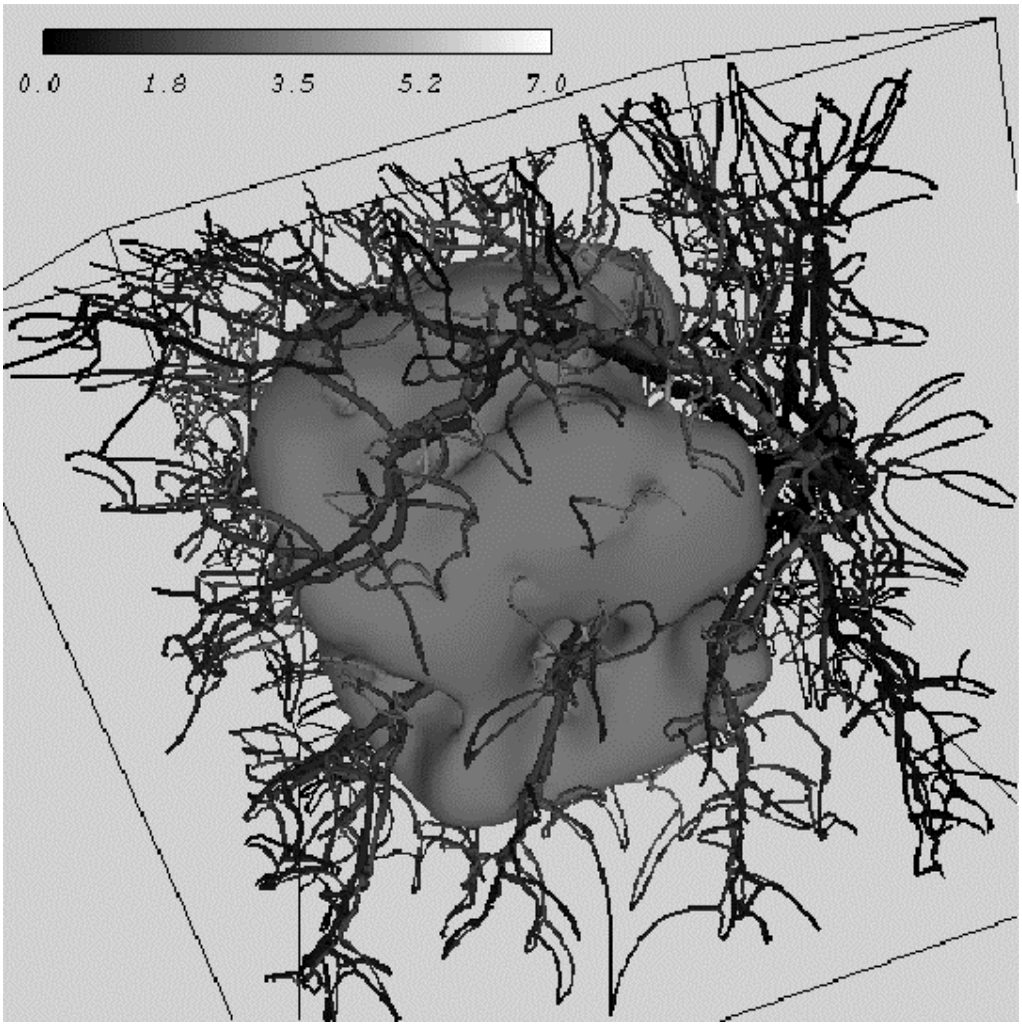
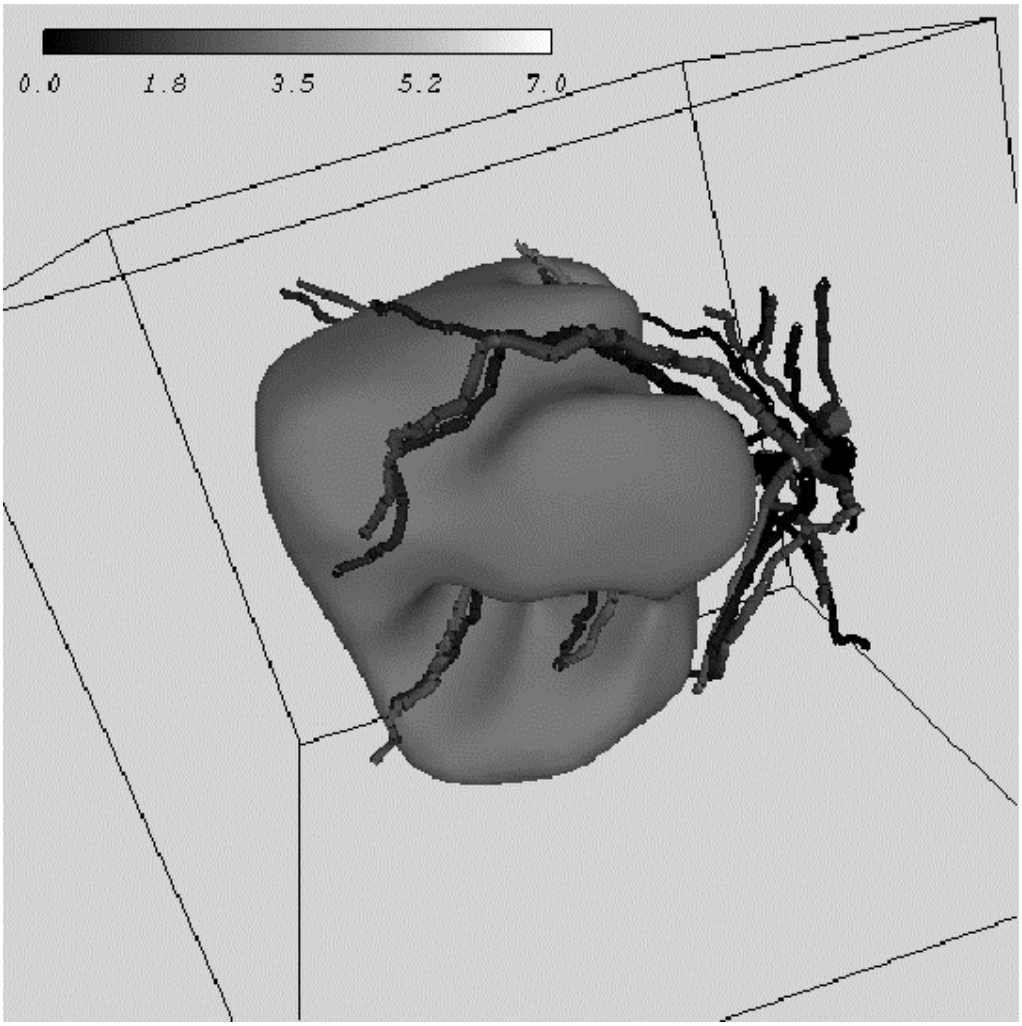


Figure 6: Temperature isosurface for temperature rise of 4 K in a heated tissue cube, in which the detailed artificial vasculature of Figure 5 is reduced to only the larger vessels.



The work in this thesis has not resulted in a nice and simple recipe for the calculation of the effective conductivity and a modified heatsink term to use for an anatomy with given perfusion and with a given amount of discrete vessels. The simulations in this thesis suggest that it will not be possible to devise such a recipe that is generally valid. The efforts have however resulted in two programs, VAMP and DIVA, that make it possible to find an answer to relevant questions in hyperthermia. For example, temperatures in tissue between hot sources can be calculated using a detailed artificial vessel network. A combined heatsink-effective conductivity description would have the benefit of simplicity and larger computational speed, but for a geometry that is considerably different from previous geometries (size of implant, spacing of sources) numerical simulations to validate the proposed heatsink and effective conductivity will be necessary.
In the clinic, at this moment the most dependable method of calculating temperatures is likewise through the expansion of the true patient vasculature by a generic vessel network that is compatible with the spatial distribution of the different tissue types.

Further investigations will be necessary to see if the thermal behaviour is overly sensitive to the characteristics of the generic expansion. Other investigators have done simulations which suggest that this is not the case, which supports the applicability of the method.