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Improvement of head and neck hyperthermia treatment planning

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Improvement of Head and Neck Hyperthermia Treatment Planning

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Graduation report performed at Erasmus MC, Unit Hyperthermia of the Radiotherapy Department

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1 Introduction

Hyperthermia, an increase of tumor tissue temperature above 40° C for more than an hour, is used as an adjuvant technique to treat tumors. Hyperthermia kills tumor cells that are poorly perfused and makes the tissue more vulnerable to ionizing radiation (radiotherapy) and chemotherapy. Moreover, the cancer tissue that is mostly affected by hyperthermia is less vulnerable for radiotherapy and vice versa, so both methods complement each other. Tissue can be heated using ultrasound, electromagnetic waves or conduction of heat. At the unit Hyperthermia of the Radiotherapy department of the Daniel den Hoed Cancer Center, electromagnetic waves are used for the application of hyperthermia. An increase in local control after 5 years, which means that no traces of the treated tumor are found, of head and neck tumors from 24% to 69% has been reported in literature for the addition of hyperthermia to RT [1]. To investigate the possibility to treat patients with head and neck tumors, the HyperCollar applicator was built. It has 12 patch antennas that are uniformly distributed on 2 rings. By adjusting the amplitude and the phase of the signals per antenna, the required interference pattern to heat the tumor can be created.

Because the head and neck region contains many tissue transitions and critical tissues like the spinal cord, hyperthermia treatment planning (HTP) is necessary for finding the optimum amplitudes and phases of the antennas. For HTP, firstly a 3 dimensional (3D) CT-scan of the required section of the patient is made. Then the CT-slides are semi-automatically converted into tissue distributions. Different tissues are given their corresponding electromagnetic properties (permeability, conductivity and permittivity); this results in the 3D patient model (PM). Secondly the PM is, together with a CAD model of the applicator, imported in a simulation platform (SEMCAD X) [2] and the electromagnetic fields are computed. Thirdly, a thermal algorithm can be used for extracting a heat distribution from the computed interference pattern and the PM. Fourthly, the heat distribution is computationally optimized by searching the best fitted amplitude and phase of the 12 antennas for the best heating ability. Currently, the thermal algorithm is not yet developed and/or verified to be used for HTP. Instead, the specific absorption rate (SAR) distribution is used to optimize the settings. SAR, a value depending on the RMS value of the electric field and the properties of the tissue, is often used to quantify the electromagnetic energy absorbed by tissue. As optimum SAR pattern used in this thesis, the ratio of SAR in the tumor with respect to SAR in healthy tissue is maximized.

The influence of several parameters on the accuracy of HTP is unknown. Among these parameters are the influences of numerous SEMCAD X's settings. The most important parameters are the choice of EM solver from the pallet that SEMCAD X provides, and the influence of different grid settings on the EM results. Therefore, in this report the effect of these settings on the SAR distribution are investigated. A second issue of HTP for the HyperCollar that is investigated in this thesis is that the predicted optimum SAR pattern often does not cover the complete tumor at the desired intensity level. One of the identified reasons for this is a non-optimal optimization functional, or just because of too little parameters that can be varied. Three methods to improve the SAR coverage of the tumor will be investigated in the second part of this report: the use of an internal EM source, the use of time reversal and the use of dynamic SAR steering.

This thesis is organized as follows. In chapter 2, an introduction of the head and neck applicator of the Daniel den Hoed Cancer Center is given, together with a explanation
of the treatment planning. In chapter 3, the different Finite Difference Time Domain (FDTD) implementations of SEMCAD X are discussed. In section 4.2, an investigation of the influence of grid settings and antenna rotation of the antenna on SAR is given. In section 4.3 an evaluation is given of the influence of PM resolution on the resulting SAR outcome. Chapter 5 provides an evaluation of some possible methods to improve the SAR pattern, quantified by percentage of tumor coverage or by the ratio of SAR in the tumor with respect to the SAR in healthy tissue. Finally, in chapter 6, recommendations resulting from the research as presented in this report are given.
2 The HyperCollar and treatment planning

2.1 The HyperCollar

When treating cancer in the head and neck region with hyperthermia, some difficulties have to be faced. The head and neck region consists of many tissue transitions and many healthy critical tissues which are sensitive to heat, like the spinal cord and the brains. Furthermore, large cooling vessels can counteract the induced heat. Recently, an applicator was built that is specifically designed to overcome these difficulties [9]. It provides sufficient degrees of freedom to both maximize the power absorption in the tumor as well as to limit the power delivered in critical heat sensitive healthy tissue. The HyperCollar consists of 12 patch antennas placed uniformly over 2 rings of 6 patch antennas. The antennas are designed to work at 433 MHz, a frequency that was selected in an extensive parameter study [9] and because this frequency is an ISM frequency: a frequency allocated for industry, science and medicine.

Water is used as medium between the antennas and the patient so the energy is efficiently coupled into the patient and also the skin of the patient is cooled. To achieve this in practice, a waterbolus that consists of a thin rubber-like balloon which holds the water is used. The antennas are completely submerged in water and the water thus forms the substrate of the antenna. Moreover, the water cools the antennas. The waterbolus must be placed around the patient, tight-fitting the patients skin for the above mentioned reasons and to avoid the creation of hot spots on the skin by small volumes of air.

![Figure 1: Picture of the HyperCollar, top left the ring containing the 12 patch antennas](image)

2.2 Hyperthermia treatment planning (HTP)

Treatment planning for the HyperCollar with SEMCAD X is used to find an optimal configuration for the amplitudes and phases of the signals of the 12 antennas. Because the incorporated thermal solver that accounts for flow in vessels is not
validated enough to be reliable for HTP, the SAR is used for HTP and throughout this thesis (Eq. 1), which is defined as follows:

$$SAR = \frac{\sigma_{eff} |E_{tot}|^2}{2\rho},$$  \hspace{1cm} (1)

with SAR in W/kg, $\sigma_{eff}$ the effective electrical conductivity in S/m, $\rho$ the density of the tissue in kg/m$^3$ and $E_{tot}$ the root mean square value of the electric field.

HTP for the HyperCollar requires that a model of the head and neck region of the patient is created using a MRI/CT-scan. These scans are segmented in different tissue types and electromagnetic (EM) properties at 433MHz (which are found in literature) are assigned to the respective tissues. The resulting patient model (PM) is placed in a 3D SEMCAD X model of the applicator, shown in Fig. 2. The EM field of each antenna of the HyperCollar is computed, and superposition of all antenna contributions applying their respective weight factors gives $E_{tot}$ (Eq. 2):

$$E_{tot}(r) = \sum_{i=1}^{3} \sum_{k=1}^{12} A_k E_i(r) e^{i\phi_k},$$  \hspace{1cm} (2)

with $I$ the vectorial component of the electric field $E$ and $A_k$ and $\phi_k$ the amplitude and phase of the signal at antenna $k$.

A SAR optimization algorithm, described in [10], is used to calculate the optimal amplitude and phase for every antenna by maximizing $I$ in Eq. 2.2

$$I = \frac{\overline{SAR}_{Target}}{\overline{SAR}_{AllTissues}},$$  \hspace{1cm} (3)

with $\overline{SAR}_{Target}$ and $\overline{SAR}_{AllTissues}$ the mean SAR in the target and the whole tissue respectively. The resulting SAR is normalized to a total of 1 Watt input power (for all antennas) and is averaged over one gram of tissue, to remove high SAR values in the absorption pattern due to the approximation of the PM by voxels according to the IEEE Standard C95.3-2002. This averaged SAR is called the spatial peak SAR. The two methods to evaluate the result of the optimization are a cumulative SAR histogram of the spatial peak SAR and an iso-surface plot. The cumulative SAR histogram is a function of the volume fraction as a function of the SAR level. Using this plot, one can read out which percentage
of a volume receives a certain spatial peak SAR value. For HTP for the HyperCollar, the value of 25% of the maximum of 1 gram averaged spatial peak SAR in the PM is used as the assumed effective dose. $TC_{25}$ (tumor coverage) is defined as the percentage of the tumor which receives this dose and can be obtained from the cumulative SAR histogram. An iso-surface plot of the area where the spatial peak SAR is equal or greater than 25% of the maximum spatial peak SAR ($ISO_{25}$) is used to qualitatively visualize the applied dose.
3 Choosing the best FDTD implementations in SEMCAD X

3.1 EM solvers as used by SEMCAD X

SEMCAD X [2] is an EM simulation software package based on the Finite Difference Time Domain (FDTD) method. It provides multiple types of solvers to simulate a model. The solvers of interest for HTP are the conventional FDTD, as currently used in HTP for the HyperCollar, the ADI-FDTD solver and the conformal FDTD solver. Previously, no research has been performed into the benefit of using these other solvers and therefore the purpose of this chapter is to discuss these solvers in more detail, and their potential benefit in HTP for the HyperCollar. All simulations in this thesis are carried out using SEMCAD X.

3.2 The Finite Difference Time-Domain method (FDTD)

In 1865 Maxwell formulated a set of equations which described the behavior of electromagnetic fields in time domain. For an isotropic medium they can be denoted in differential form by:

\[ \nabla \times \bar{E}(r, t) = -\frac{\partial \bar{B}(r, t)}{\partial t}, \]  
\[ \nabla \times \bar{H}(r, t) = \frac{\partial \bar{D}(r, t)}{\partial t} + J_E(r, t), \]  
\[ \nabla \cdot \bar{D}(r, t) = \rho(r, t), \]  
\[ \nabla \cdot \bar{B}(r, t) = 0. \]  

where \( \bar{E} \) is the electric field, \( \bar{B} \) the magnetic flux density, \( \bar{H} \) the magnetic field, \( \bar{D} \) the electric displacement, \( J_E \) the current density, \( \rho \) the charge density, \( t \) denotes time and \( r \) denotes the position vector defined as

\[ r = x \mathbf{u}_x + y \mathbf{u}_y + z \mathbf{u}_z \]  

where \( \mathbf{u}_x, \mathbf{u}_y, \mathbf{u}_z \) are the Cartesian unit vectors. The constitutive relations are:

\[ \bar{B}(r, t) = \mu \bar{H}(r, t) \]  
\[ \bar{D}(r, t) = \varepsilon \bar{E}(r, t) \]  
\[ \bar{J}(r, t) = \sigma \bar{E}(r, t), \]  

where \( \mu \) the permeability, \( \varepsilon \) the permittivity and \( \sigma \) the conductivity and are described by

\[ \varepsilon = \varepsilon_0 \varepsilon_r \]  
\[ \mu = \mu_0 \mu_r, \]  

with \( \varepsilon_0 \) and \( \varepsilon_r \) the free space and relative permittivity and \( \mu_0 \) and \( \mu_r \) the free space and relative permeability. No magnetic materials are used in this thesis, so \( \mu_r = 1. \) The FDTD method is often used to solve the Maxwell equations. The FDTD method approximates the derivatives in Eq. 4 by "finite difference" approximations. Yee ([3]) proposed to use
a spatially staggered grid consisting of rectangular cells of same size to solve the FDTD equations. Two grids are used in Yee’s method, one defining the locations where the electric field is computed and one grid defining the locations where the magnetic field is updated. Both grids are spatially staggered with respect to each other by half the length of the cell size as depicted in Fig. 3. Therefore the simulation set-up must be divided in brick like blocks; called Yee-cells (Fig. 3) or voxels. To keep the FDTD method explicit, the electric and magnetic field updates are temporally shifted, which means that a magnetic field update is done between two electric field updates in time. Every field component $F_{\alpha}^{n}_{i,j,k} = (t,x,y,z)$ in FDTD can be denoted by:

$$F_{\alpha}^{n+1}_{i,j,k} = F_{\alpha}(n\Delta t, i \Delta x, j \Delta y, k \Delta z),$$

where $\alpha=x,y$, or $z$; $n$ is the time index and $i,j,k$ are space indices. $\Delta t$ is the time step and $\Delta x, \Delta y$ and $\Delta z$ the spatial steps along the respective axis. This results in the explicit finite difference equations which are for the x-direction:

$$E_x^{n+1}_{i,j,k} = C_A E_x^n_{i,j,k}$$
$$+ C_B \left[ \frac{H_z^{n+\frac{1}{2}}_{i,j,k} - H_z^{n+\frac{1}{2}}_{i,j,k-\frac{1}{2}}}{\Delta y} - \frac{H_y^{n+\frac{1}{2}}_{i,j,k+\frac{1}{2}} - H_y^{n+\frac{1}{2}}_{i,j,k-\frac{1}{2}}}{\Delta z} \right],$$

and

$$H_x^{n+\frac{1}{2}}_{i,j,k} = H_x^{n-\frac{1}{2}}_{i,j,k}$$
$$+ \frac{\Delta t}{\mu(i,j,k)} \left[ \frac{E_y^n_{i,j,k+\frac{1}{2}} - E_y^n_{i,j,k-\frac{1}{2}}}{\Delta z} - \frac{E_z^n_{i,j,k+\frac{1}{2}} - E_z^n_{i,j,k-\frac{1}{2}}}{\Delta y} \right],$$

Figure 3: Figure showing the grids for the electric and magnetic fields
where

\[ C_A = \frac{1 - \frac{\sigma_{i,j,k} \Delta t}{2 \varepsilon_{i,j,k}}}{1 + \frac{\sigma_{i,j,k} \Delta t}{2 \varepsilon_{i,j,k}}} \quad (11) \]

\[ C_B = \frac{\frac{\Delta t}{\varepsilon_{i,j,k}}}{1 + \frac{\sigma_{i,j,k} \Delta t}{2 \varepsilon_{i,j,k}}} \quad (12) \]

Similar expressions can be derived for \( E_y, E_z, H_y \) and \( H_z \). In Fig 4 the staggering of the electric and magnetic field update in time is shown.

\[ \text{Figure 4: This figure shows the staggering in time of the electric and magnetic field updates.} \]

**Stability of FDTD**

The FDTD-method is only conditionally stable, meaning that there is an upper bound to the time step. This upper bound is, for non-dispersive media, related to the smallest cell size via the Courant-Friedrichs-Lewy (CFL) criterion:

\[ \Delta t < \frac{\varepsilon \mu}{\sqrt{\frac{1}{\Delta x^2} + \frac{1}{\Delta y^2} + \frac{1}{\Delta z^2}}} \quad (13) \]

This criterion immediately clarifies one of the weaknesses of FDTD: a small cell size is necessary when small structures must be simulated, leading to a small time step and long simulation times. A simulation with an antenna that is modelled by voxels of size 3x3x3mm will have a three times larger time step than a simulation of the same antenna with voxel size 1x1x1mm. A three times larger time step lowers the amount of needed updates of every six field components \( (E_x, E_y, E_z, H_x, H_y, H_z) \) by a factor 3, thus a theoretical reduction of computation time by a factor 18.

**Hardware acceleration**

Simulations can have many cells and time steps. In order to solve these equations more quickly, SEMCAD X offers a speeding up of the computation by using a hardware accelerator card (Axware), which is basically a GPU. The speedup with the hardware accelerator used for HTP for the HyperCollar is about 8 times compared to a CPU.

### 3.3 The Alternating Direction Implicit FDTD method (ADI-FDTD)

One of the major disadvantages of the FDTD algorithm is that it is only stable if the CFL-condition in Eq. 13 is satisfied. This means that using a fine grid, which is necessary for high resolution HTP (with small \( \Delta x, \Delta y, \Delta z \)), results in a small time step and therefore a large computation time. To overcome this, the ADI-FDTD method has been developed:
an unconditionally stable scheme. The time step of ADI-FDTD can be made as large as possible, however the resulting error increases with growing time step. The ADI-FDTD scheme uses the same spatial grid as the conventional FDTD uses, however the electric and magnetic field updates are not staggered in time. According to the company that sells SEMCAD (SPEAG), a speed up of 10 times can be achieved. For the computation of both the electric field and the magnetic field, an intermediate (non-physical) field at half the time step \((n + \frac{1}{2})\) is computed. The equation to compute the electric field at time \((n + \frac{1}{2})\) is:

\[
\frac{E_x^{n+\frac{1}{2},j,k} - E_x^{n,j,k}}{\Delta t/2} = \frac{1}{\varepsilon} \left[ \frac{H_z^{n+\frac{1}{2},j+\frac{1}{2},k} - H_z^{n+\frac{1}{2},j-\frac{1}{2},k}}{\Delta y} - \frac{H_y^{n,j+\frac{1}{2},k} - H_y^{n,j,k}}{\Delta z} \right],
\]

and the equation to compute the electric field at time \(n+1\) is:

\[
\frac{E_x^{n+1,j,k} - E_x^{n+\frac{1}{2},j,k}}{\Delta t/2} = \frac{1}{\varepsilon} \left[ \frac{H_z^{n+\frac{1}{2},j+\frac{1}{2},k} - H_z^{n+\frac{1}{2},j-\frac{1}{2},k}}{\Delta y} - \frac{H_y^{n+1,j,k} - H_y^{n+1,j,k}}{\Delta z} \right].
\]

Note that in Eq. 14 the first approximated derivative is computed implicitly, whereas in Eq. 15 the second approximated derivative is computed implicitly. Similar expressions can be written for \(H_x, E_y, H_y, E_z\) and \(H_y\).

Solving this implicit scheme requires the inversion of matrices and, according to SPEAG, this can not be done efficiently using the GPU and therefore no hardware acceleration is (and will) be available for SEMCAD X’s ADI solver. The advantage of a shorter computation time is diminished if a hardware accelerated FDTD solver is used and therefore ADI-FDTD will not be investigated in this report.

### 3.4 Conformal FDTD

Because in the FDTD method the spatial environment is divided into rectangular cells, small structures with boundaries not aligned to the grid cannot be gridded exactly. This is called the staircasing effect. To overcome this problem, conformal gridding was developed. The basis of this method is that the voxels that contains a boundary are still treated homogeneously. However, effective EM properties are used to average between the two solids in that voxel in order to compute the fields more accurately. SEMCAD X uses different conformal schemes for PEC/dielectric and dielectric/dielectric boundaries.

**Possible use of the Conformal FDTD in HTP**

The conformal FDTD method as implemented in SEMCAD X gives some errors in voxel-\(ing\) the model, for example some voxels have wrong material properties. Moreover, when using conformal voxel-\(ing\) for the patch antennas the feeding pin is incorrectly modelled (see Fig. 5). Therefore, there is need for more research, beyond the scope of this thesis, and the conformal FDTD will not be investigated in this report. However,
conformal FDTD is a promising technique and is expected to improve the FDTD results especially in the case of PEC with edges not aligned to the grid as is the case with HTP for the HyperCollar.

![Figure 5](image)

**Figure 5:** Voxelling of the patch antenna using the conformal gridder, showing the small error made in modelling the feeding pin.

**PEC/dielectric transition**
If a grid cell contains an edge dividing a PEC and a dielectric object, the effective PEC-free length and PEC-free area (see Fig. 6) is taken into account, and the electric field is scaled accordingly, stored and used in the original FDTD update equations. An extensive derivation can be found in [8], but a short summary of the method is given below: SEMCAD X uses for conformal FDTD method almost the same algorithm as for conven-

![Figure 6](image)

**Figure 6:** Face of a voxel containing both PEC and dielectricum, showing the PEC-free lengths $L_y$ and $L_x$ and PEC-free area $A_z$
tional FDTD, with a few minor adaptations. The H-field update equation is

$$H_{x|_{i,j,k}}^{n+1/2} = H_{x|_{i,j,k}}^{n-1/2} + \frac{\Delta t}{\mu \cdot A_{x|_{i,j,k}}^{ratio}} \left( \Delta z \left( \begin{array}{c} E_{y|_{i,j,k+1/2}}^{n} \cdot \Delta_{y|_{i,j,k}}^{ratio} - E_{y|_{i,j,k-1/2}}^{n} \cdot \Delta_{y|_{i,j,k}}^{ratio} \\ E_{z|_{i,j,k+1/2}}^{n} \cdot \Delta_{z|_{i,j,k}}^{ratio} - E_{z|_{i,j,k-1/2}}^{n} \cdot \Delta_{z|_{i,j,k}}^{ratio} \end{array} \right) \right)$$

where

$$A_{x|_{i,j,k}}^{ratio} = \frac{A_{x|_{i,j,k}}}{\Delta y \Delta z}$$
$$A_{y|_{i,j,k}}^{ratio} = \frac{A_{y|_{i,j,k}}}{\Delta y \Delta z}$$

are the effective PEC-free relative area and edge ratio, respectively. It is more convenient to transform Eq. 16 into the conventional update FDTD equation (10), and therefore the term $\mu \cdot A_{x|_{i,j,k}}^{ratio}$ is stored instead of $\mu$ and instead of $E_{\alpha}$ (with $\alpha=x,y,z$), $E_{\alpha} \Delta_{\alpha}^{ratio}$ is stored. The update equation of the electric field is exactly the same as in the conventional FDTD scheme (Eq. 9, modified in a similar manner, but the update coefficient $C_B$ is multiplied by $\Delta_{\alpha}^{ratio}$. The advantage of this approach is that, for conformal FDTD, no additional computational effort is needed.

Stability of conformal PEC FDTD
In [8] a stability criterium for the SEMCAD X implementation of the conformal PEC FDTD method is derived. Because the applied conformal method uses the same update equation as the conventional FDTD, although with modified material parameters, the original time step calculated by the CFL-criterium can be adapted for conformal FDTD by multiplication with a certain factor which is explained in details in [8].

Dielectric/dielectric transition
If a voxel contains more than one dielectric solid, the update equations are modified using the effective material properties. For example: for two dielectric solids in one voxel, the effective electric permittivity of the voxel is

$$\varepsilon_{eff} = A_{1}^{ratio} \cdot \varepsilon_1 + A_{2}^{ratio} \cdot \varepsilon_2.$$  

where $A_{\alpha}^{ratio}$ is the ratio of the area of that specific dielectricum on the face of the voxel and the total area of the face of the voxel.

3.5 Meshing in FDTD

Uniform gridding
Uniform gridding means that the spatial steps $\Delta \alpha$ with ($\alpha=x,y$ or $z$) have the same size. For spatially large computations, this often results in too many voxels to possible compute. To overcome this the grid generating algorithm of SEMCAD X allows for non-uniform
Graded gridding in the FDTD method
Graded gridding is a gridding method to locally use a higher resolution at a specific place, e.g. at an antenna. The spatial environment in the direction of all three orthogonal axes in the region of interest is globally refined with a finer grid, while the rest of the environment is coarser which saves memory and computation time. The rate of size change between neighboring cells should, by experience, not exceed 1.3 to ensure stability of the FDTD algorithm. A downside of this graded grid technique is the larger error due to numerical dispersion. In this thesis, only graded gridding is used. Because the fact that the grid of the refined local region refines the grid in all three orthogonal axes (in the complete computational domain), and because in this thesis the influence of voxel size variation on a EM simulation is investigated, sometimes tricks must be applied to overcome the influence of a local refinement on the grid in the varied voxel region.

Figure 7: This shows the effect of graded gridding; the fine grid is due to the antenna and it is seen that the refinement is along all axes (x,y,z)

Subgridding in the FDTD method
Subgridding means that the grid in a rectangular subdomain is locally refined with a higher resolution. The advantage compared to a graded grid is that the grid outside the region of interest can be coarser, hence unlike the graded gridding, the refinement does not apply to the whole computational domain. This comes at the expense of interpolation errors. Currently, subgridding is not yet operational in SEMCAD X, and will therefore not be used in this report.

3.6 Discussion
Using the conformal FDTD method, antennas can possibly be coarser gridded than using the conventional FDTD. This will result in a lower amount of voxels and a larger minimum time step, which can reduce computation time of HTP. If no hardware accelerator is available, the ADI FDTD method can be used to lower computational time of HTP. The used simulation models (hyperthermia device and PM) in HTP are large and need small voxels for the antennas and the use of uniform gridding will lead to too large simulations to be practical \( \gg 10 \) Mvoxels, and therefore graded gridding has to be used for HTP.
4 The influence of FDTD grid settings on the SAR accuracy

In Chapter 3, the different solvers that SEMCAD X provides and their benefit for HTP, have been discussed. The influence of the FDTD settings on the HTP results will be investigated in this chapter. Because many settings influence the accuracy of the FDTD method and not all settings can be investigated in this thesis, only the influence of voxel-elling on HTP results is investigated in this thesis. The reason for this choice is that the voxel-elling is assumed to have the most influence on the FDTD EM simulations of HTP. Moreover, knowing the influence of voxel size on HTP is important for finding an optimum trade-off between HTP accuracy and computation time. This chapter is organized as follows: in Section 4.2 the influence of antenna voxel-elling on HTP is reported, whereafter in Section 4.3 the influence of PM voxel-elling is shown.

4.1 Materials and methods

The gamma method

A method known as the gamma method [6] is used for comparing two different spatial SAR distributions. The gamma method allows the comparison of two different spatial SAR distributions in terms of both dose-difference (DD) and distance-to-agreement (DTA). DD specifies the percentage in which the two distributions are allowed to disagree in SAR, whereas DTA specifies the distance in which the two distributions are allowed to disagree.

Firstly, for a point \(i\) in the reference distribution (REF) the spatial distance with all its surrounding points in the distribution-under-test (DUT) is computed:

\[
 r(\hat{r}_{\text{DUT}}, \hat{r}_{\text{REF},i}) = |\hat{r}_{\text{REF},i} - \hat{r}_{\text{DUT}}|.
\]

This is done for all points \(i\) in the REF. Secondly, for a point \(i\) in the REF, the SAR difference with all its surroundings in the DUT is computed:

\[
 \delta_{\text{SAR}}(\hat{r}_{\text{DUT}}, \hat{r}_{\text{REF},i}) = \text{SAR}(\hat{r}_{\text{REF},i}) - \text{SAR}(\hat{r}_{\text{DUT}}),
\]

and this is also done for all points \(i\) in the REF. Next, for every point \(i\) in the REF, a distribution function \(\Gamma\) is computed that relates Eq. 19 and Eq. 20 to the acceptance criteria:

\[
 \Gamma(\hat{r}_{\text{DUT}}, \hat{r}_{\text{REF},i}) = \sqrt{\frac{r^2(\hat{r}_{\text{DUT}}, \hat{r}_{\text{REF},i})}{\text{DTA}^2} + \frac{\delta^2(\hat{r}_{\text{DUT}}, \hat{r}_{\text{REF},i})}{\text{DD}^2}}.
\]

Finally, for every point \(i\) in the REF a \(\gamma\) value is computed, which is the minimum of \(\Gamma\) for that point:

\[
 \gamma(\hat{r}_{\text{REF},i}) = \min \{ \Gamma(\hat{r}_{\text{DUT}}, \hat{r}_{\text{REF},i}) \} \forall \hat{r}_{\text{DUT}}.
\]

If \(\gamma \leq 1\) at point \(i\) it means that the criteria DD and DTA are met at point \(i\). In this thesis, it is assumed that a good agreement is achieved when 95% of the points in the \(\gamma\) distribution is within the used DD and DTA constrains. Thus \(\gamma_{95} \leq 1\).
Influence of interpolation on the gamma evaluation

The results of the gamma evaluation depends on the spatial distance of all points in the (interpolated) distribution of the simulated model. In literature, it is advised to use a minimum spatial distance between neighboring values of DTA/3. Define the refinement (rf) as (Eq. 23):

\[ rf = \frac{DTA}{IntStep} \]  

(23)

where IntStep is the spatial distance between neighboring values. In this investigation the \( \gamma_{95} \) of two fields is computed using various refinement steps, see Fig. 8. From this figure it is shown that \( \gamma_{95} \) is stable for \( rf \geq 6 \), which is in line with the rf found in [6] and therefore rf is chosen 6 throughout this thesis. A remark must be made that all reference and tested distributions are exported out of SEMCAD X using a python script that automatically interpolates the distributions. This approach will introduce an extra interpolation error resulting in an error in the \( \gamma_{95} \) values. However because this effect is assumed to be small in comparison with the differences caused by the varied grid parameter, it will be neglected. The reason why a python script is used to export the values out of SEMCAD X is because this script allows the export of a user specified spatial block.

**Figure 8:** \( \gamma_{95} \) as a function of the refinement factor \( rf \). The used setup is the same as used in this section, for \( \phi = 0^\circ \); a simulation with a maximum voxel size of 1 mm is used as reference and a simulation with a maximum voxel size of 10 mm is the tested simulation. The same evaluation block is used as in Fig.14. The tested criteria are DD=5% and DTA=5mm.

**Selection of the DD and DTA criteria**

Finding appropriate DTA and DD criteria for HTP is difficult, because the gamma method
has never been used for HTP for the HyperCollar and hence, no information on the obtainable accuracy of the simulated SAR distribution with the true SAR is available. In radiotherapy, DTA and DD values of 3mm and 3% respectively are considered feasible, however this is for comparison with a measured distribution. Moreover, the gamma method, as used in this thesis, computes the difference of a SAR distribution with a reference simulation and with only one varying parameter, namely the voxel size of the antenna. The accuracy of current HTP is influenced by many factors, like the positioning of the patient, incorrect modelling of the waterbolus, use of SAR instead of temperature and many others. Therefore a small error of a few mm in simulated SAR distributions will be overshadowed by the other parameters on the hyperthermia treatment which are likely to be in the cm range. As a result, in this thesis the chosen agreement criteria that are acceptable are DTA=3mm and DD=3%.

**Influence of grid settings on the resulting grid**

SEMCAD X contains two grid generators, the interactive gridder and the conventional gridder. The conventional gridder provides the best control with respect to input settings and will therefore be used throughout this investigation. Despite this, the grid generator of the conventional gridder (and the interactive gridder) behaves somewhat as a black box, so it is not possible to totally control the grid and to completely understand the effect of a gridder parameter on the resulting grid. Therefore, the effect of a varied parameter on the resulting grid must be investigated. The parameters that the conventional gridder offers to influence the grid are:

- Maximum and a minimum voxel size for every solid
- Refinement at the edges of solids
- The grading ratios
- Possibility to add baselines

The maximum voxel size and the minimum voxel sizes provide boundaries on voxel sizes for the gridder, whereas a refinement factor at the edges lowers the minimum voxel size at the edge of a solid by a user-defined refinement factor. The grading ratio gives the maximum difference in size of neighboring voxels in all three directions. The baselines are spatial boundaries where voxel edges are enforced and are placed automatically by the gridder. However, three options exists for the automatic placing of the baselines, namely "Using edges" and "Using bounding box" and "automatic". The "Using edges" option places the baselines on the edge of the solid, spatially delimiting all edges of the antenna, while the "bounding box" option places the baselines on the edges of a rectangular block that exactly fits the antenna. The "automatic" option chooses the "Using edges" option for voxelling the patch antennas and results in a more accurate geometrical voxelling of the antenna, at the expense of a finer grid and thus a longer computation time.

Not all gridding parameters of SEMCAD X have been investigated. Because adding baselines is done automatically by the gridder and manually adding baselines during real HTP will be too time consuming, the influence of baselines on the EM outcome will not be investigated. The grading ratio in all three directions is often chosen about 1.3 to ensure stability, therefore no investigation on the grading ratio is carried out in this report. For
a real HTP model with 12 antennas refinement on edges results in too many voxels to be practical (>9M voxels), so no investigation on the influence of refinement on edges is carried out. The evaluation of the influence of the maximum and the minimum voxel size of the antennas on the amount of voxels of a real HTP model revealed the following: only the maximum voxel size has a significant impact on the grid. This behavior is also seen if only a simple block of material is used as model. Also, when inspecting the resulting grid when the maximum voxel size of the antenna is varied, the grid does not change much anymore when the maximum antenna voxel size is above 5 mm.

4.2 Influence of antenna voxelling on HTP for the HyperCollar for conventional FDTD

The influence of a FDTD grid parameter on the resulting optimized phase/amplitude and $TC_{25}$ of a complete HTP requires many large simulations. Because SAR is used as the optimization parameter for HTP (see Chapter 2), the evaluation is simplified by only considering the influence on the SAR distribution when a single FDTD grid parameter is varied. For this investigation, a simplified version of a HTP setup is used: the patient’s neck is modelled as a layer of muscle of 100 mm and the ground plane is modelled as a straight ground plane instead of the bent ground plane of the HyperCollar, to simplify the voxelling and to to minimize the effect of the ground plane voxelling on the results. The height of the muscle layer is chosen 150 mm to match the spatial distance between a real patient and the patch antenna. Only one patch antenna is used and it is located in the middle of the model. The ground plane is 400 by 400 mm, large enough to minimize (too) small ground plane effects. The model is shown in Fig. 9.

Figure 9: Setup for evaluating the influence of grid settings on the SAR results.
Influence of patch orientation in the HyperCollar on the voxelling

In HTP the HyperCollar is always placed aligned with the grid in the xy-plane as shown in Fig. 10. $\phi$ is defined as the angle of rotation around the z-axis. Because of rotational symmetry, it is assumed that a rotation of the patch at $\phi = 15^\circ$ and $\phi = 75^\circ$ result in the same voxelling (the rotation with respect to the orthogonal axis of the grid is $15^\circ$ for both patches). Extending this idea, from Fig. 10 it can be seen that the effect of rotation of the patches on the voxelling can be observed by only considering patch rotations of $\phi = 15^\circ$ and $\phi = 45^\circ$ (because all patch antennas in the HyperCollar have a rotation of $15^\circ$ or $45^\circ$ with respect to the orthogonal axis of the grid). In this thesis, also a rotation of $30^\circ$ will be considered, because this value lies in between $15$ an $45$ degrees, and is interesting for future applicators having different patch orientations than the current HyperCollar.

4.2.1 Method

Because of the lack of verification possibilities (no measurement of the electric field, analytical model or other simulation program with a different scheme than FDTD available),
it is chosen to use a simulation with a finely voxelled patch with the patch aligned to the grid, as the reference. The patch in the reference simulation is uniformly voxelled with a cubic voxel size of 0.1 mm and this simulation is assumed to be the most accurate. Then, the EM field of the setup as depicted in Fig. 9 is computed for varying maximum cubic voxel sizes of the patch for four different rotation angels $\phi = 0, 15, 30$ and $45$ degrees (the complete model is rotated). The frequency is 433 MHz, as used in HTP for the HyperCollar and the baseline mode is set to "automatic" (see 4.1). The larger the maximum voxel size of the patch, the coarser the voxels of the antenna will be.

*Comparison using the resonance frequency*

As an initial step, broadband simulations were used and the resonance frequency, the frequency where the inductance and capacitance of the antenna cancel each other, was used as an evaluation. The patch antenna is designed to be resonant at 433 MHz, and the quality of the FDTD voxelling influences the resonance of the patch. Results are depicted in Fig. 12. Fig. 12 shows a sharp decrease in resonance frequency for maximum voxel sizes larger than 1 mm, however in the resulting electric field, no large difference was seen for maximum voxel sizes larger and smaller than 1 mm, hence simply stating that 1 mm is the optimum maximum voxels size is not possible. The larger influence of the maximum voxels size on the situation aligned to the grid (0°) is due to the baselines forcing the voxels to be smaller in the rotated cases, hence the influence of varying the maximum voxel size on the grid is less significant in the rotated situations than in the situation aligned to the grid.

*Comparison using the deviation in electric field*

Then, the electric field of the simulations was compared with a fine reference field using Eq. 24:

$$\xi = 100 \times \frac{|E_{RMS} - E_{RMS}|}{|E_{RMS}|},$$

(24)

where $\xi$ the mean deviation in percent, $E_{RMS}$ the root mean square electric(RMS) field under test and $E_{RMS}$ a fine RMS reference (again of a simulation with an uniformly
Figure 12: Resonance frequency versus maximum voxel size of the patch antenna; The upperbound and lowerbound are taken ±2 MHz with respect to the reference simulation (an uniformly voxelled patch with a cubic voxel size of 0.1 mm aligned to the grid).

voxelled patch with a cubic voxel size of 0.1 mm aligned to the grid) electric field. \( \xi \) is depicted in Fig.13.

However, this investigation does not say much about the effect on HTP, where SAR is the evaluated value. Moreover it is difficult to draw conclusions from Fig.13 because it is hard to give criteria for \( \xi \) that need to be met. Therefore the gamma method was used.

Comparison using the gamma method The resulting SAR distribution is compared with the reference SAR distribution using the gamma method. Because the gamma method is a computationally intensive task, especially for low DTA values, the evaluated space is chosen to be a square block of 15x15x15 mm located in the muscle, just at the interface between water and muscle. The height of the square is chosen to be just inside the muscle layer, where the SAR is supposed to be the highest. To minimize the influence of the
Figure 14: This figure shows the location of the evaluation block, designated by the arrows.

grid on the voxels in the evaluation block due to the graded gridding (see Chapter 3), the block is not located above the centerline of the patch, but 27.5 and 47.4 mm shifted in the positive x and y direction (from feeding pin to the center of the evaluation block)
respectively as shown in Fig. 14. When the model is rotated by $\phi = 0, 15, 30$ and 45 degrees, the evaluation block is also rotated. This ensures that always the same spatial data with respect to the patch antenna is evaluated. The results of this investigation are depicted in Fig. 15. In Fig. 15 the $\gamma_{95}$ is plotted as a function of the maximum voxel size for angles $\phi = 0, 15, 30$ and 45 degrees. The line that indicates whether the criteria are met ($\gamma_{95}=1$) is also shown. The obtained $\gamma_{95}$ values are quite high and the DD and DTA criteria of 3% and

3mm are not met for the rotated simulations. However by plotting the gamma distribution in 3D it was established that the highest gamma values, thus largest disagreement were located at the bottom of the evaluation block, see Fig. 16. When the gamma method is applied to SAR distributions in the evaluation block, neglecting the lower 5 mm of data (at the bottom of the evaluation block), to minimize the effect of different voxel properties due to staircasing on the boundary between water and muscle, the $\gamma_{95}$ values are recomputed and the results are shown in Fig. 17. In the previous investigation, the maximum voxel size of the patch antenna was varied using the option to automatically place the baselines. This results in too many voxels of practical use for HTP (>10 Mvoxels). To investigate the effect of a coarser patch voxelling than currently done with HTP, the same investigation as previously is carried out, but now using the "bounding box" option to place the baselines. This results in patch antenna voxelling as used in current HTP, where the "bounding box" option is always enabled. This time, only rotations of 15 and 45 degrees with respect to the grid are considered, because these situations can be distinguished from the HyperCollar (see 4.1). The evaluation block is the same as shown in Fig. 14, but without the lower 5 mm and the considered maximum voxel sizes are 1, 2, 5 and 10 mm. Again, the simulation

![Figure 15: Agreement ($\gamma_{95}$) as a function of the maximum voxel size (mm) for different rotation angles of the patch.](image-url)
Figure 16: \( \gamma \) distribution for the 30 degrees rotated grid (max. voxel size=10)

with fine patch voxelling aligned to the grid is used as a reference.

4.2.2 Results

Results are depicted in Fig. 18.

4.2.3 Discussion and Conclusions

One would expect the \( \gamma_{95} \) value to rise more or less exponentially with increasing maximum voxel size of the patch antenna. However this is not the case (see Fig. 17 and Fig. 18). One of the reasons is the in 4.1 mentioned effect that the grid does not change much for maximum voxel sizes larger than 5 mm. Therefore the SAR distributions are also expected not to change much, explaining the stabilization of the \( \gamma_{95} \) for the larger maximum voxel sizes. At a maximum voxels size of 1 mm for a rotation of \( \phi = 45^\circ \), the high \( \gamma_{95} \) values are found. These high \( \gamma_{95} \) values are caused by a strange voxelling effect: above the centerline of the patch (if the model was not rotated), at the boundary between water and muscle, voxels that should be given the properties of muscle are given the properties of water, which results in a large difference in SAR distributions compared to the reference simulation. This happens only in this particular case and therefore the \( \gamma_{95} \) value at a maximum voxel size of 1 mm and a rotation of \( \phi = 45^\circ \) is neglected. The rotation \( \phi \) of the patch antenna has a large influence on the SAR distribution. The criteria DTA=3mm and DD=3% are never met (\( \gamma_{95} > 1 \)) for a rotation of \( \phi = 15^\circ \). Because the HyperCol-
Figure 17: $\gamma_{95}$ as a function of the maximum voxel size (mm) for different rotation angles of the patch, when the lower 5mm of the evaluation block is ignored.

It was found that the SAR difference between a simulation with a finely voxelled patch as reference and simulations with varying maximum voxels size of the patch is too large to meet the criteria DTA=3mm and DD=3% for antenna rotations of $\phi = 15$ and 45 degrees.

4.3 Influence of PM voxelling on HTP for the HyperCollar for conventional FDTD

The goal for this section is to investigate the influence of varying the voxel size of a patient model (PM) on HTP for the HyperCollar and finding two different accuracy levels for voxeling the PM in a real HTP: one for a coarse grid and one for a fine grid. This makes it possible to choose between a fast (for the coarse grid) and a more accurate (for the fine grid) HTP.
Figure 18: $\gamma_{95}$ values for the 30 degrees rotated grid (max. voxel size=10), when the lower 5 mm of the evaluation block is ignored and the "BoundingBox" option is enabled.

Again, the problem is simplified by not investigating the results on the complete computational domain of a HTP, but by evaluating the difference in SAR distribution with the gamma method as described in 4.1. For this investigation, a real and large PM is used in simulations for a varying cubic voxel size. In order to use a fine and a coarse grid for HTP the used criteria for the gamma method are DTA=3mm and DD=3% for the fine grid and DTA=5mm and DD=5% for a coarse grid.

4.3.1 Method

The setup is constructed of a PM and a single antenna Fig. 19, the background is given the properties of water to resemble the waterbolus. The antenna is located to the right of the PM, at a distance of 8 cm from the skin (see Fig. 19), as could be the case for a real HTP. Only one antenna is used to cancel the effect of interference on the resulting SAR pattern. This investigation requires the voxels of the PM to be independent of the voxelling of the antenna. Because a graded grid is used, the finer antenna voxelling influences the voxelling of the PM. To minimize this effect, the setup was constructed as follows:

- A dipole antenna is used that requires less voxels instead of using an HyperCollar patch antenna.

- The set-up is rotated $\phi = 45^\circ$ with respect to the grid, thus the effect of the orthogonal grid refinement caused by the antenna is located outside the PM, see Fig. 20.
• The conventional grider is used in the simulations and its settings are exported to the interactive grider, providing results as shown in Fig. 21.

The size of the cubic voxels of the PM are varied from 2 mm to 14 mm and a simulation with a PM voxelling of voxel size 1 mm is used as a reference. For the evaluation, the gamma method is used. The evaluation with the gamma method is done on a block of 15x15x15 mm located in the tumor of the patient, which is a tumor of the nasopharynx type (located behind the nasal cavity, see Fig. 22). Normalization is done as in HTP, to 1 Watt input power for the computed source power at 433MHz. This means that the SAR is computed after the simulated electric field is multiplied by a factor $\frac{\sqrt{1}}{\sqrt{P(f_0)}}$, where $P(f_0)$ is the real part of the computed source power (when the input signal has an amplitude of 1 Volt) at a frequency of 433MHz.

![Figure 19: Used set-up, patient model and dipole.](image)

4.3.2 Results

In Fig. 23 the $\gamma_{95}$ values for the 2 tested criteria are given as a function of the PM voxel size. The $\gamma_{95} = 1$ is also indicated.

4.3.3 Discussion and Conclusions

Fig. 23 shows a linear dependence of the $\gamma_{95}$ value on the voxel sizes of the patch. From these results, the maximum PM voxel size for a high resolution HTP is 6 mm. The line of DD=5% and DTA=5mm crosses the $\gamma_{95} = 1$ line at a PM voxel size of 13 mm, however for assuring that the criteria of DD=5% and DTA=5 mm are always met, it is assumed that the linear dependence holds for a PM voxel size above 9 mm, hence a PM voxel size
Figure 20: The PM and the grid implementation. This figure shows that the grid refinement caused by the antenna is located mainly outside the PM.

Figure 21: Showing the voxels of the PM at cubic voxel sizes of 1, 4, and 11 mm.

of 10 mm is chosen for the PM voxel size of a low resolution HTP. However, because it is unknown where the highest differences in SAR distribution are, the choice of evaluation block location makes this a case study on itself. For further research, it is interesting to evaluate the gamma distribution on the whole PM so the values of highest SAR differences will be revealed.

Conclusions
Based on the used criteria of DD=3% and DTA=3mm, a maximum PM voxel size of 6 mm must be used for a high resolution HTP, whereas a maximum PM voxel size of 10 mm must be used for a HTP with low computation time, based on the criteria of DD=5% and DTA=5mm.
Figure 22: This figure shows the location of the tumor in the head with respect to the antenna.

Figure 23: $γ_95$ as a function of PM voxel size
5 Methods to improve the SAR patterns

In this chapter, some possible methods to improve the SAR pattern quality are discussed. Currently, the optimized SAR pattern of HTP is quantified by $TC_{25}$ (see Chapter 2). From previous treatment plannings, it is known that the resulting $TC_{25}$ of an HTP for the HyperCollar is often less than 75%. Assuming that $TC_{25}$ represents the true thermal dose given, 75% is too little to treat the whole tumor, and improvement is mandatory. The quality of the SAR pattern can also be expressed in terms of mean SAR in the target with respect to mean SAR in all tissue (aSAR). aSAR is in this thesis defined as [9]:

$$aSAR = \frac{SAR_{target}}{SAR_{all}}$$  \hspace{1cm} (25)

where $SAR_{target}$ is the mean SAR in the target and $SAR_{all}$ is the mean SAR in all tissue.

Three possible options to increase SAR coverage will be explored in this thesis:

- The use of an additional intraluminal EM source
- Dynamic SAR steering (DS)
- Optimization by time reversal (reciprocity)

5.1 An additional intraluminal EM source

An additional antenna, placed intraluminally in the patient might improve the SAR pattern in terms of both coverage and aSAR. An advantage of this method is that the antenna will be closer to the tumor than the HyperCollar antennas are, and therefore more SAR can be coupled into the tumor, in terms of both coverage and aSAR. The additional antenna might also be used to minimize SAR values in healthy tissue, allowing the use of more power by the HyperCollar.

This technique requires the development of a new antenna that can be fit into the patients pharynx or larynx through the nose or the mouth. The influence of different locations of the antenna on the resulting SAR optimization pattern has to be investigated. The accurate positioning of the additional antenna is an issue, but in the difficult to heat nasopharynx region (behind the nasal cavity), this can be solved by using a nasopharynx mould [11]. The nasopharynx mould is a flexible catheter that is inserted backwards into the mouth of a patient and then pulled back through the nasal cavity, hence with the rear end coming out of the nose. The mould conforms well to the patients nasopharynx and is thus, when inserted, fixed and the correct location of the antenna can be found using a CT-scan. For optimal coupling, the direction of the electric field of the intraluminal antenna should be aligned with the direction of the electric field of the HyperCollar, hence aligned with the patient axis. This option is only theoretically explored because the idea of using a nasopharynx mould to fix the antenna came to late to include a simulation in this thesis.

5.2 The dynamic SAR steering

Experience has shown that for large tumors, the SAR focus ($ISO_{25}$, see Chapter 2) at 433 MHz is too small to cover the whole tumor. Moreover, the occurrence of hotspots limits
the amount of power that can be applied and thus the height of the tumor temperature. During treatment, the power is increased until the patient complaints about pain caused by occurring hotspots. Usually, the goal of a homogenous tumor temperature of 43°C is never reached before a pain complaint. The idea of DS is to quickly switch between multiple phase/amplitude settings during treatment, thereby adding degrees of freedom to better heat the total tumor. Further, hotspots can potentially be spread out over healthy tissue, which allows the use of more power to increase the tumor temperature. Among others, DS requires:

- Highly accurate and in the clinic reproducible HTP.
- Sufficiently fast switching between phase/amplitude settings of the hyperthermia device to ensure that the temperature in the tumor does not decrease too much between settings.
- An optimization method to compute the foci.

The goal of this section is to investigate whether the in SEMCAD X implemented SAR optimization algorithms can be used for computing the foci.

5.2.1 Materials and methods

The Generalized Eigenvalue (GE) optimizer

At the moment, two algorithms to optimize aSAR are available and implemented in SEMCAD X: a Genetic algorithm [12] and an algorithm based on generalized eigenvalues [10] [12]. Both algorithms maximize the aSAR and also provide comparable results, so only the generalized eigenvalue algorithm is used in this investigation.

Region masks

Region masks are virtual (not voxelled) geometrical objects that can be used for postprocessing. In this investigation, region masks are used to specify additional sensitive regions and additional target regions (instead of the tumor) for the GE optimizer.

Cumulative Histogram

Besides $TC_{25}$, also cumulative histograms are used for evaluation. A cumulative histogram is a 2D plot showing which ratio of a certain volume (like muscle, brain or total

Figure 24: The nasopharynx mould; the right part of the mould is, when inserted, located above the mouth
head) receives a certain amount of SAR. For example, the ratio of tumor volume that receives $TC_{25}$ can be read out from this cumulative histogram.

**Method**

In this chapter the potential of the generalized eigenvalue algorithm for dynamic SAR steering is investigated. Hereto, a case study is done on a real PM. This specific PM is chosen because it includes a very large tumor that by a single SAR pattern was only partially covered with the $ISO_{25}$. In this early stage of investigation regarding DS, the hyperthermia device is assumed to have an infinitely small switching time between various phase/amplitude settings. This assumption simplifies the investigation by leaving out the rate of tissue cooling, so a simple addition of the optimized SAR patterns for various settings provides a total SAR pattern, that can be compared to the SAR from a single setting.

A focus ($ISO_{25}$) at a certain location can be obtained by setting a region mask surrounding this location as the target for the GE optimizer. The resulting focus can be spatially steered by using multiple region masks in the tumor to optimize on. If the tumor is divided into region masks, multiple GE optimizations (one optimization for every region mask) will give multiple, spatially spread foci. Such a region mask can have every geometrical shape, size and location. However, for this investigation only one geometrical shape and size for the region mask is considered i.e. a cube with edges of 40mm. Using infrared measurements, the 50% iso-SAR focus ($ISO_{50}$) for the HyperCollar in a homogeneous muscle equivalent phantom is found to have a width (in the transverse plane) of 35 mm and a length (in the sagittal and coronal plane) of 90 mm [9]. However, in a PM, this focus is often more spread due to the many tissue transitions. Moreover, in HTP and in this investigation $ISO_{25}$ is used to determine the focus, which will result in a even more spread focus.

To ensure that the optimized foci overlap, the complete tumor and its surroundings are divided into 18 cubical regions masks with 40 mm ribs, as depicted in Fig. 25. The

![Figure 25: Patient model used for the case study. Left shows the patient in the HyperCollar; red is the tumor. Right shows the division of the tumor in target regions](image)

model in Fig. 25 is computed as currently done during HTP and aSAR is optimized with the whole tumor as target region ("Whole Tumor Opt"). From the optimizations for all
cubical region masks, only the optimizations that sufficiently added to the total spatial coverage of the tumor with $ISO_{25}$ without adding substantial SAR in healthy tissue were selected. This was done by visual inspection of the $ISO_{25}$ SAR patterns of every region mask optimization separately. From the 10 selected optimizations, the SAR patterns are normalized to 1 Watt real input power and spatially combined using a Python script. The resulting SAR pattern is analyzed using a cumulative histogram and compared with the cumulative histogram of the "Whole Tumor Opt" distribution, see Fig. 26.

![Cumulative Histogram](image)

**Figure 26:** The dotted line is tumor, the squared line is all tissue; Above the cumulative histogram the "Whole Tumor Opt", under the cumulative histogram of the SAR pattern from DS. The "0" marker denotes the $TC_{25}$. The major difference in the scale on the x-axis between both figures is due to the overlapping of the 10 used SAR patterns in the lower figure.
5.2.2 Results

The cumulative histograms shows that, for the “Whole Tumor Opt” optimization, 76% of $TC_{25}$ covers the tumor, while a value of 93% of $TC_{25}$ is obtained using dynamic steering. In Fig 27 the resulting $ISO_{25}$ contour plots are visualized, showing clearly the larger focus and, hence, better coverage using the DS.

![Coronal view, Sagittal view, Axial view](image)

**Figure 27:** $ISO_{25}$ without and with dynamic steering (DS)

5.2.3 Discussion and Conclusions

Using the generalized eigenvalue algorithm, it is feasible to find multiple settings that combined lead to a better $TC_{25}\%$ using cubical region masks of size 40 mm. However, handpicking the useful optimizations will take too much time during real HTP and therefore the method must be implemented in an automatic procedure. Also it is not investigated whether comparable or even better results can be obtained using other sizes, shapes and locations of the region masks. Using DS, the maximum amount of different optimization settings that can be used depends on the rate of tissue cooling and the performance of the applicator in terms of the time it takes to stabilize after an optimization update. A note must be made that the coverage using DS is not the true coverage, because the problem was simplified by assuming an infinite switching speed. The true performance of DS can only be seen when cooling is accounted for, which requires the conversion of the SAR to the true temperature.

**Conclusions**

This investigation showed that the GE algorithm can be used to find multiple SAR foci for DS using cubical region masks of size 40mm. By adding up of SAR, the foci increased $TC_{25}$, for the used case, from 76% to 93% without a dramatic increase of hotspots.
5.3 The use of Time Reversal

The downside of using the generalized eigenvalue algorithm for finding the optimal control settings [10] as used in current HTP is the lack of total TC$_{25}$ of the tumor. The aSAR is optimal, however this does not mean that the best total tumor coverage is found. To overcome this problem, a new method based on SAR coverage using the reciprocity (time reversal) of antenna radiation ([13]) is investigated in this chapter. The idea of using time reversal to find optimum phase and amplitude settings is as follows. If one or more source antenna(s) are placed inside the tumor and the antennas of the applicator are treated as receivers, the received signals will have a time delay and an amplitude corresponding to the location and shape of the tumor and anatomy. If the received signals are time reversed and transmitted by the applicator back to the tumor, the interference will be optimum at the location of the source(s). Besides a possibly better SAR coverage, another advantage of this method is the decrease in required computation time because only one simulation is necessary, instead of one simulation per antenna as in the current treatment planning procedure. The disadvantage is that, if a reoptimization is required, it takes another complete simulation of the total field instead of a much faster re-weighting of the fields in the antennas.

5.3.1 Materials and methods

Used Setup

To more quickly explore the benefit of optimization using reciprocity, a simple 2D model of a neck surrounded by eight uniformly divided dipole antennas is used. Because SEM-CAD X is a 3D simulation package, the model is stretched out like a cylinder. Dipole antennas are used to approximate the applicator because they are relatively easy to model. The shape of the tumor is chosen to be elongated from the center to the outside of the model, because this shape is proven to be difficult to cover with SAR using the generalized eigenvalue method (Fig. 28). The background is assigned properties of water. The sources that are placed in the tumor are hard sources, (the electric field at the source is independent of reflections), placed along the axial direction of the model at the height of the dipoles. The hard sources can be seen as dipole antennas, without the need of using additional PEC material and thus reducing computation time. The GE optimizer as described in Section 5.2.1 is used and the cumulative histogram as explained in Section 5.2.1 is used as evaluation method. The configuration of Fig. 28 is simulated for all eight antennas separately at 433MHz, and then optimized using the genetic eigenvalue algorithm, with the tumor as target. Also, two simulations are done using time reversal. For the first simulation one source was placed at the center of the tumor (Fig. 30) and, for the second simulation, nine sources were considered in the tumor (one placed at the center and the other eight at the edge of the tumor), see Fig.31. The latter is used to investigate whether accounting for the tumor geometry provides better results. The received amplitude and phases of the dipole antennas are time reversed and applied to the dipole antennas as a source by computing $E_{tot}$ (Eq. 2) using the simulated EM-fields for all antennas separately.
5.3.2 Results

The result from the generalized eigenvalue is depicted in Fig. 29; the result of time reversal using one source is depicted in Fig. 30 and the result using nine sources is depicted in Fig. 31.

5.3.3 Discussion and Conclusions

In a two-dimensional setup, it is clearly seen that in terms of coverage the reciprocity has an advantage compared to the generalized eigenvalue algorithm. The coverage increased from 55% of $TC_{25}$ using the genetic eigenvalue method to 100% of $TC_{25}$ using reciprocity and one source. Moreover, if the sources are also placed at the surface of the tumor, the 50% ISO SAR value ($TC_{50}$) increases from 45% using one source to 50%, which indicates that further investigation of the source placing is needed to obtain better results. However, all this comes at the expense of more hotspots (see Fig. 30 and Fig. 31) and only temperature simulations can predict whether this is a bottleneck. Recommended is to investigate the benefit of reciprocity for HTP in a real 3D PM model using the HyperCollar. When using a 3D PM model the 2D reciprocity is extended to 3D and patch antennas are used instead of dipole antennas. The latter is not assumed to give a different outcome because the patch antenna has similar radiation properties as a dipole antenna. The use of patch antennas will probably not give a different outcome, because the patch antennas has similar radiation properties as a dipole antenna.

For the used 2D model time reversal improved the 50% ISO SAR value ($TC_{50}$) from 25% using the GE optimizer to 45% using time reversal with one source placed in the middle.
Figure 29: Results using the generalized eigenvalue method; the blue line represents tumor, the green line represents all tissues of the tumor. If nine sources are used, one placed at the center and the other eight at the edge of the tumor, $TC_{50}$ increased to 50%.
Figure 30: Results using time reversal with one source; the blue line represents tumor, the green line represents all tissues.
**Figure 31:** Results using time reversal with multiple sources placed around the edge; the blue line represents tumor, the green line represents all tissues.
6 Conclusions and recommendations

The first part of this thesis investigates the influence of the most important solvers and grid settings that SEMCAD X provides for use in HTP for the HyperCollar. It was found, that when no hardware accelerator is available, the SEMCAD X ADI FDTD solver can be used to lower computational time. From this thesis it can be concluded that using conventional FDTD, a SAR accuracy of DD=3% and DTA=3mm can not be achieved for HTP for the HyperCollar.

The second part of this thesis investigates the possibility to improve SAR distributions. In this part of the thesis it was found, that for a 2D setup, time reversal resulted in a higher $TC_{25}$ than the GE optimizer did. Also, it was found that the GE optimizer is able to find multiple foci (ISO$_{25}$) using region masks, which is helpful for the investigation of DS.

6.1 Future research

The lack of analytical solutions or measurements makes it difficult to draw conclusions of the true SAR accuracy, therefore it is recommended to do measurements. The gamma method provides a strong tool to test these measurements with simulations.

Because large differences are found in $\gamma_{95}$, the overall accuracy can be concluded to be much lower than the checked criteria DTA=3mm and DD=3%. If one wants better accuracy (criteria DTA<3mm and DD<3%), the HTP simulations need to be improved for different antenna rotations. This might be done by rotating the complete HTP model, so that for every simulation the enabled patch is aligned with the grid. However this is not considered feasible within the current SEMCAD X framework. Another solution would be to develop a new antenna that lowers the influence of rotation on the FDTD method, for example a dipole antenna. However, measurements are indispensable for a real comparison. If lowering computation time of HTP is the goal, then considering the large spreading of $\gamma_{95}$ it is advised to look at the HTP results for much coarser voxelling of the antennas than currently done in HTP for the HyperCollar. The conformal FDTD can then be tested for its ability to compensate for the coarser resolution, hence lowering the amount of needed voxels even more. The investigation of the grid on a 3D PM (chapter 4.3) shows that the segmentation of a PM from CT-slices, which is very time consuming, can be less accurate for SAR based HTP resulting in a speed-up in segmentation.

The 2D Time Reversal investigation shows that a better SAR optimization in 2D can be obtained. Currently, in HTP the coverage of $TC_{25}$ is often lower than 75% and if time reversal shows that a better coverage can be obtained, it is likely that an algorithm based on coverage will give higher $TC_{25}$ coverage results, and should be developed. Chapter 5 also proves the possibility to use the Generalized Eigenvalue method for DS. However because of the inability of the Generalized Eigenvalue method to exactly specify the location of the focus, this brute force method gives a uncertainty in the outcome of the HTP optimization. Therefore, it is recommended to develop an optimization method that has the ability to specify the location of the focus on forehand.
7 References

References


