

APPLICATION OF NUMERICAL MODELING TECHNIQUES IN ELECTROMAGNETIC HYPERTHERMIA

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Abstract

Electromagnetic hyperthermia has been demonstrated to be a safe and useful adjuvant to ionizing radiation in the treatment of malignant tumors. However, applicators and systems for delivering the optimum treatment prescribed by the physicians are far from being available at present. Computer modeling can play a significant role in the design of better heating equipment and in improving the quality of the hyperthermia treatments currently being administered. There is an active ongoing research to develop suitable calculational models using a variety of numerical techniques. But several gaps exist in the current knowledge regarding the validity of these numerical simulations in the clinical context. The development of treatment planning systems similar to those used for radiation therapy requires resolution of these issues. Of the different numerical modeling approaches currently being developed, the finite-difference time-domain (FD-TD) technique has been extensively applied to calculate specific absorption rate (SAR) patterns in complex 3-D heterogeneous biological objects primarily because it is accurate and has a small computer burden relative to frequency-domain integral equation and finite-element techniques. Following a brief review of the historical development of numerical modeling of electromagnetic interaction with biological structures in the hyperthermia context, examples of recent calculations using FD-TD technique in realistic situations in electromagnetic hyperthermia are provided. It has been observed from 2-D calculations, that the water bolus, routinely used in the clinic to provide energy coupling and surface(skin) temperature control, and the inhomogeneous tissue structures significantly modify the SAR patterns compared to patterns computed in planar and homogeneous structures. In conclusion, future areas of work are identified and discussed.

Introduction

Computation of electromagnetic (EM) field interaction with biological objects have been extensively carried out over the past three decades primarily to quantify specific absorption rates (SAR) from a health hazard point of view [Durney, 1980; Spiegel, 1984]. In recent years the application of these numerical techniques in electromagnetic hyperthermia has become an active area of research [Strohbehn and Roemer, 1984]. Based on a number of clinical studies it has been established that hyperthermia, i.e. heating of tumors to temperatures greater than 42°C, can produce increased cell killing and act as an efficient adjuvant to ionizing radiation therapy in the treatment of localized superficial malignancies [Arcangeli et al, 1988; Overgaard, 1989].

At present, heating techniques using EM energy are commonly employed in the clinic to produce therapeutic temperatures in the tumor [Hand and James (eds), 1986]. The ideal objective is to heat all tumor tissues to a specified temperature without overheating surrounding normal tissues. In virtually all the clinical situations encountered, it is extremely difficult to know that adequate coverage has been achieved. A number of factors influence the EM power deposition patterns from commonly used applicators. Significant among these are the effect of relative applicator positioning with respect to the defined treatment volume, and the means of coupling the energy from the commonly used flat or planar aperture applicators to the irregularly contoured patient surface. Thin-walled plastic bags containing stationary or circulating distilled water are routinely

used in the clinic as bolus between the applicator and the treatment surface for improving the coupling efficiency and to provide surface cooling where required. In most instances, due to the curved geometry of the body contour, the bolus bag tends to be distorted resulting in asymmetrical loading of the applicator. Also, the integral type bolus used with some commercially available applicators can produce a collimation effect that alters the power deposition patterns. It is virtually impossible to intuitively visualize or measure the effects of these factors on the power deposition patterns. To obtain experimental 3-D power deposition patterns for all the situations encountered in the clinic is a time-consuming and difficult task.

Alternatively, computer modeling of hyperthermia treatments to predict SAR distributions would be extremely useful for pretreatment evaluation of suitable applicator set-up that will provide adequate coverage of the treatment volume. Such computerized simulation of hyperthermia treatments would be especially valuable in deep tumor treatments where the absorbed power patterns are further modified by complicated internal tissue structures [Wust et al, 1991]. For example, Sathiaseelan et al [1986] used a 2-D numerical method of moments (MoM) model to investigate the effect of phase steering for an annular phased array (APA) applicator system. The results of this numerical study were then used in the clinic to devise phase steering techniques for the APA to change the deposited power patterns to improve the quality of treatments and reduce toxicity [Howard et al, 1986]. Also, numerical modeling studies would enable extensive parametric studies to be performed quickly and inexpensively so that sensitive and insensitive parameters can be identified. These studies will also help to evaluate the multi-applicator array systems that are being developed to provide better coverage. Another useful area is in the design of applicators. Numerical modeling can be used as a computer-aided design tool in testing different designs quickly thus saving time [Shaw et al, 1991; Iskander and Tumei, 1989]. However, there is a considerable need for research in this area and only recently software tools have become available for determining three-dimensional power deposition and temperature patterns for realistic patient anatomies. The current state of research in this area have been excellently reviewed and discussed in a recent publication on *Thermal Dosimetry and Treatment planning* [Gautherie (ed), 1990].

Detailed EM power deposition calculations have been performed so far using 2-D models and attempts are currently being made to develop detailed 3-D heterogeneous models. Although 2-D models have been useful, they imply "cylindrical type" structures when extrapolated to the real 3-D situation, and thus do not accurately model the biological system. However, the experimentally demonstrated effect of variations in anatomical configurations [Turner, 1984] suggests that 3-D numerical methods which take into account the overall interaction of the body with EM fields are required to accurately predict EM power deposition. Following a brief review of the historical development of numerical modeling of electromagnetic interaction with biological structures, examples of recent calculations using FD-TD technique in realistic clinical situations will be provided. Future area of work will be discussed in conclusion.

EM Modeling Background

In the 1970's and early 1980's, detailed predictive models of EM wave absorption by biological tissue structures were based largely on Harrington's frequency-domain method of moments (MoM) [Harrington, 1968]. Here, an integral or integro-differential equation is derived from Maxwell's equations either by enforcing the continuity of tangential electric/magnetic fields across dielectric media boundaries [Poggio and Miller, 1979], or by applying the concept of polarization currents to specify wave fields within the interior of dielectric objects [Richmond, 1965]. 3-D volumetric formulations of MoM using space-filling cubic [Livesay and Chen, 1974] and tetrahedral [Schaubert et al, 1984] elements have been formulated primarily for application to the biological tissue interaction problem. Yet, because MoM leads to systems of linear equations having dense, full, complex-valued coefficient matrices, the required computer storage has an N^2

dependence, where N is the number of field unknowns; and the required computer execution time to solve the MoM system has an N^2 to N^3 dependence. With spatial resolution requirements in the order of 0.1 to 0.2 wavelength to avoid aliasing of vital near-field magnitude and phase data, this implies that MoM modeling of arbitrary 3-D structures spanning more than a very few wavelengths would tax or exhaust even the most capable existing computers.

The literature indicates that the basic MoM treatment of whole-body human tissue structures culminated in models having in the order of several hundred discretization cells, each of multi-centimeter scale [DeFord et al, 1983]. This is clearly inadequate to provide levels of detail of internal tissue structure needed for hyperthermia treatment planning. Theoretical efforts therefore shifted to examine alternative formulations of MoM which promise a dimensional reduction of computer resources. One such formulation [Borup and Gandhi, 1984] exploits the convolutional nature of the volume integral equation based on polarization currents (when defined on a uniform grid or lattice) to permit use of the fast Fourier transform (FFT) in the solution algorithm. Although, in principle, extending the horizon of MoM modeling to structures having thousands of discretization cells, the literature indicates that this approach may provide substantial errors in the calculations of the internal fields in biological tissues for EM excitations having transverse electric (TE) field components [Borup et al, 1987]. This would greatly impede application of FFT approaches to the important 3-D tissue case.

An alternative to frequency-domain MoM formulations of EM wave penetration into biological tissues was the FD-TD method introduced by Taflove in 1975 [Taflove and Brodwin, 1975], based in part on an algorithm published by Yee [Yee, 1966]. FD-TD is a direct finite-difference solution of Maxwell's time-dependent curl equations which implements a sampled-data reduction of the continuous EM field in a volume of space over a period of time. Overall, FD-TD is a marching-in-time procedure which simulates the continuous actual waves by sampled-data numerical analogs. At each time step, the system of equations to update the field components is fully explicit, so that there is no need to set up or solve a set of linear equations. This feature permits the required computational resources to vary approximately as N , the number of field unknowns in the model, which is dimensionally low compared to that of the original MoM formulation and the finite element method. Further, this feature permits highly efficient processing of the FD-TD algorithm by both vectorizing and concurrent-processing supercomputers such as the Cray Y-MP/8 and the Intel Delta, respectively. Studies are beginning to emerge where detailed energy deposition patterns are being calculated inside inhomogeneous three-dimensional models of the body [Sullivan et al, 1988; Sullivan, 1990; Wang and Gandhi, 1989].

Unlike the FFT/MoM approaches, which also have dimensionally-low computer burdens, FD-TD has been shown to be robust, providing highly accurate modeling predictions for a wide variety of EM wave interaction problems in two and three dimensions [Taflove, 1988; Taflove and Umashankar, 1989]. A subset of these includes biological tissue interactions: detailed (order 1-cm resolution) whole-human-body dosimetry under plane-wave illumination [Sullivan et al, 1988], and detailed partial- or whole-body hyperthermia modeling [Lau et al 1986a; Sullivan et al, 1987; Sullivan et al, 1988; Sullivan, 1990; Wang and Gandhi, 1989]. The increasing availability of Cray-type vectorizing supercomputers to the engineering electromagnetics community has in fact permitted application of FD-TD to model EM wave interactions with arbitrary 3-D structures substantially larger in electrical size than MoM (approximately 10 times larger in span and 1000 times larger in volume). As of July 1992, the largest reported FD-TD models are the set of digital interconnect structures modeled by Picket-May & Taflove [1992]. These 3-D models, implemented on the Cray Y-MP/8, solve for up to 60-million unknown vector field components.

Largely due to the demonstrated success of FD-TD grid-based computational modeling of EM wave interactions with complex structures and the clear evolutionary trends in supercomputer capabilities, interest in other "partial differential equation (PDE)" direct solvers for Maxwell's

equations has greatly expanded since the mid-1980's. These include the class of finite-element (FE) and finite-volume (FV) numerical approaches. Rockwell International Corp., in finite-volume time-domain (FV-TD) methods [Shankar et al, 1989], and Boeing Aerospace Corp., in finite-element frequency-domain (FE-FD) methods [Bussoletti et al, 1988], have developed the most advanced alternative PDE Maxwell's solvers aimed primarily at radar cross section modeling. Both the Rockwell and the Boeing efforts to find alternatives to FD-TD were motivated by the need to model target surfaces in a conformal manner. This is vital in the RCS modeling area, since the original stepped-surface or staircase approximation of smooth surfaces by FD-TD generates computational noise in the fields scattered outward to free space which markedly degrades the accuracy of the RCS calculation. There appears to be no sparse matrix algorithm available that can resolve the dimensionally-large computer burdens involved in treating the large, sparse, non-banded matrices that arise in all FE-FD approaches in 3-D. In effect, the FE-FD user generating sparse matrices must resort to matrix inversion, LU decomposition, or iterative methods historically employed by MoM users generating dense matrices. As discussed above, these matrix problems stymied the further development of MoM, and it appears likely that the further development of pure FE-FD will be likewise stymied.

Since the mid 1980's, as well, there have been efforts at FE-FD solutions of Maxwell's equations in the area of EM wave interactions with biological tissue structures [Lynch et al, 1988; Paulsen et al, 1988a; Paulsen et al, 1988b]. Similar to the radar cross section work, the goals here involve nearly conformal modeling of tissue structures using well-characterized geometry generation software. In 2-D, qualitative as well as quantitative retrospective comparisons with limited clinical data suggested that FE-FD numerical models accurately predicted the dominant capabilities and limitations of the annular array applicator and magnetic induction coil studied [Paulsen et al, 1985; Roemer et al, 1984a; Roemer et al 1984b; Strohbehn et al 1986]. In 3-D, the formulation of FE-FD for hyperthermia problems has been numerically implemented. However, because of the same sparse matrix problems experienced by Boeing in the radar cross section area, the application of the FE-FD method to 3-D hyperthermia problems has been very limited. Paulsen et al [1992] report elsewhere in this special issue, recent progress in FE-FD by computing 3-D EM field distributions in a full-body model with limited internal organs but without any skeletal structures. To avoid some of the drawbacks of the pure FE-FD method in 3-D, an alternative frequency-domain hybrid and boundary element formulation has been developed and implemented [Paulsen et al, 1988b]. To date only 3-D calculations on simple homogeneous and heterogeneous cylindrical geometries have been attempted with this approach because dimensionally unacceptable amounts of computer memory are still required for large-scale problems. This has resulted in the migration of the finite-element technique to the time domain (where matrices can be avoided, as in FD-TD) with the development of finite-element time-domain (FE-TD) methods [Lynch et al, 1988]. These should possess dimensional computer resource burdens similar to FD-TD. However, work in this area is ongoing and details concerning the accuracy and computer requirements of 3-D FE-TD models of hyperthermia relative to FD-TD have not yet appeared.

Unlike the RCS area, the rationale for conformal FD-TD modeling of biological structures relative to EM wave interactions is not justified. Detailed studies [Borup et al, 1987; Sullivan et al, 1987] have shown that simple FD-TD surface staircasing of cylindrical, layered cylindrical, and spherical tissue structures (of typical permittivity and loss) is sufficient to permit calculation of the penetrating internal fields with a high degree of accuracy compared to the exact summed eigenfunction solutions. It is observed that the EM fields penetrating a lossy dielectric structure are much less sensitive to the nature of the surface approximation of the structure than the fields scattered away from the structure into free space. This observation permits effective use of the earlier staircasing FD-TD models for computing penetrating fields in tissue structures. These have substantially reduced geometry generation requirements relative to the latest fully conformal FD-TD models based upon local Faraday's Law and Ampere's Law contour paths [Jurgens et al, 1992], and will sacrifice little accuracy.

Experimental Validation Studies

The major thrust in this field to date has been in developing the computational algorithms and checking their validity using analytical solutions or other numerical techniques for simple structures. Rigorous testing of how well the theoretical predictions compare to measured EM absorption in realistic heterogeneous human phantoms intended to simulate clinical situations has not been carried out so far. Experimental validations in simple muscle equivalent phantoms irradiated using waveguide applicators of the types employed in superficial hyperthermia have been reported for 2-D predictions [Rine et al, 1990] and 3-D predictions [Lau et al, 1986b, Sullivan, 1990], as well as for interstitial antennas embedded in homogeneous phantoms [Wong et al, 1986]. Validations have also been carried out for radiative type regional heating systems. Paulsen and Ross compared the predicted and experimental measurements at a single frequency of 70 MHz for the older APA [Paulsen and Ross, 1990] using simple 2-D models and phantoms. They obtained quantitative agreement in phantoms containing moderate complexities. Sullivan has compared the predicted and measured results along the major and minor axes of the CDRH elliptical phantom [Sullivan, 1990, Sullivan, 1991] filled with homogeneous muscle phantom tissue in an earlier work and has recently published further results using a modified CDRH phantom with inhomogeneities introduced [Sullivan et al, 1992]. Good agreement was observed between the FD-TD predicted results and the measurement results. While the existing validations are qualitatively encouraging, they have not been rigorous. In effect, they have not precisely established the uncertainty bounds in the basic FD-TD near-field physics model for the applicators in question. More research using both theory and experiment will have to be carried out to quantitatively determine these uncertainty bounds for the classes of aperture and dipole/array applicators, as well as for the class of interstitial applicators.

FD-TD Modeling for EM Hyperthermia with Realistic Geometries

The theoretical formulation of the FD-TD method and its implementation to solve directly the time-dependent Maxwell's equations has been described extensively in recent literature [Lau et al, 1986a; Sullivan, 1987; Taflove, 1988] and will not be reviewed here. Only examples of the application of the FD-TD technique in modeling EM hyperthermia with realistic geometries will be presented. The goals in these studies were to first develop the computational model starting with simple geometrical structures excited by simple radiators, and then extend the analysis to more complex structures excited by more complex radiators. By this approach it was possible to rigorously validate the computational model at different stages. As an example of a simple set up, a model of the human thigh irradiated with a waveguide applicator has been studied. 2-D and 3-D models using the FD-TD technique have been developed to run on different computing machines. 2-D models have been run on Compaq 386/25/Weitek laboratory computer, MicroVax II computer and Cray Y-MP supercomputer. The 3-D models have been mainly run on Cray Y-MP supercomputer.

The results of our 2-D and 3-D theoretical validation studies of the code have been published previously [Katz et al, 1991; Picket-May et al, 1992]. Following the good agreement obtained in these extensive validation studies, a 3-D model of the human thigh was reconstructed from a collection of 29 serial computerized tomographic (CT) images. The SAR distributions when irradiated with a waveguide applicator were then calculated. Different patterns were obtained for the 2-D and 3-D models [Picket-May et al, 1992]. Further calculations investigating the effect of the water bolus (routinely used in the clinic to provide energy coupling and skin temperature control) and the inhomogeneous tissue structures have been carried out in 2-D. These results are presented in this paper. In these studies a high-resolution (5-mm uniform mesh size) 128 x 100 cell FD-TD grid was analyzed. All data were obtained after time stepping 15 periods of the incident wave at 915 MHz.

Waveguide applicator excitation of a planar phantom in 2-D

Muscle equivalent planar phantoms are routinely used in the clinic to characterize the performance of applicators [Chou et al, 1986]. The measured SAR patterns are then used for treatment planning and quality assurance purposes. To test the accuracy of the FD-TD model and also to study the effect of the water bolus on the SAR distributions, planar phantom /applicator configuration with and without the water bolus was studied in 2-D at 915 MHz.

The aperture size of the applicator modeled was 10 x 10 cm. It was assumed to be filled with a low-loss dielectric material having a relative permittivity, ϵ_r , of 6 and conductivity, σ , of 0 S/m. The thickness of the water bolus used was 2.5 cm, and the water was assumed to have $\epsilon_r = 80$ and $\sigma = 0$ S/m. The dielectric properties used for muscle were $\epsilon_r = 50.5$ and $\sigma = 1.307$ S/m.

The calculated normalized SAR distributions are shown in Figures 1a and 1b. The patterns look qualitatively very similar to measured patterns. The introduction of the water bolus did not make any significant changes in the SAR distributions.

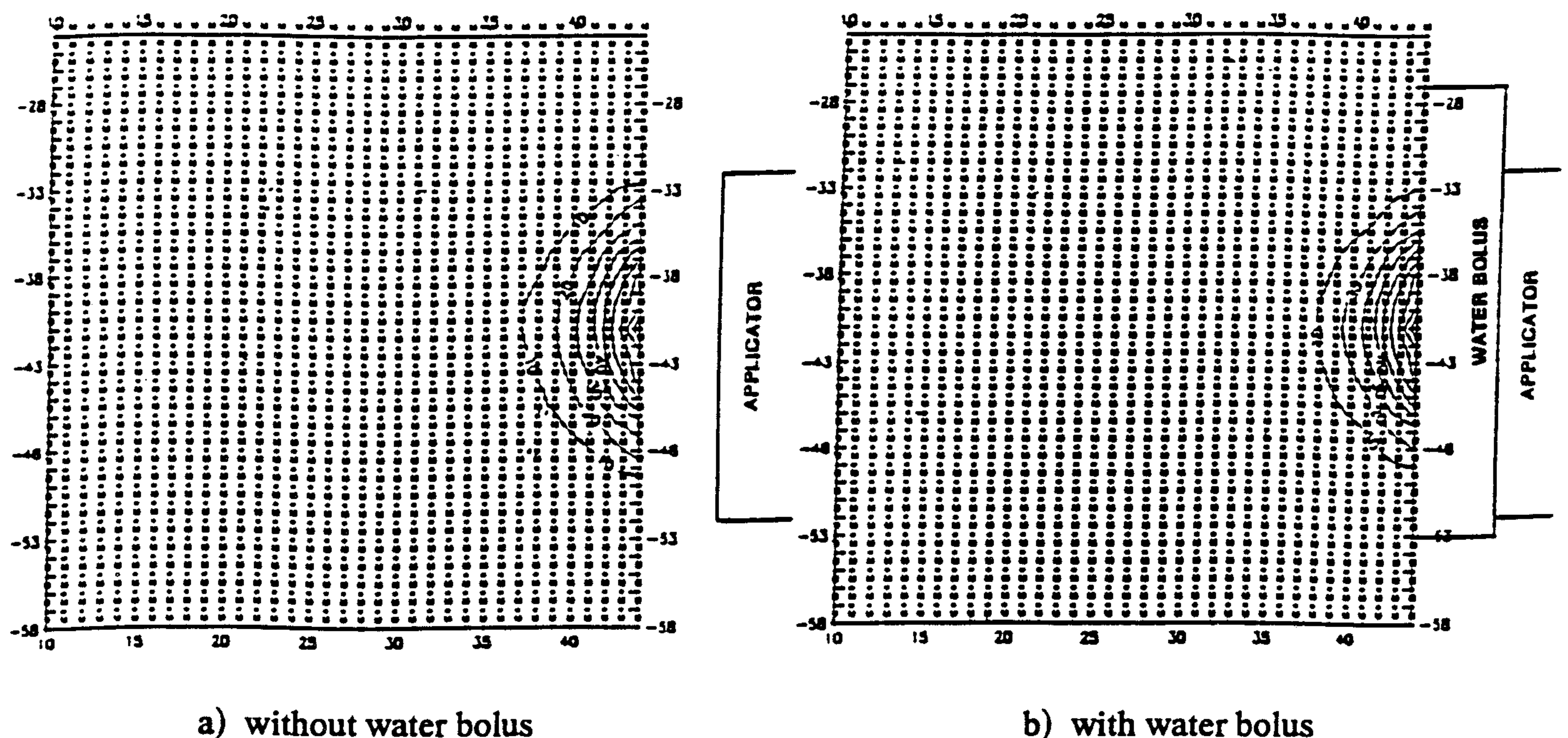


Figure 1. Normalized percent SAR distributions in a planar phantom

Waveguide applicator excitation of homogeneous and inhomogeneous thigh model in 2-D.

Using actual CT-scan data of a human thigh, the tissue structure (fat, muscle, bone, and bone marrow) was semi-automatically deduced as described in [Piket-May et al, 1992]. The thigh was assumed to be made up of homogeneous muscle in the first calculations. In Figures 2a and 2b normalized SAR distributions obtained without and with the water bolus are shown. Figures 3a

and 3b show the corresponding patterns when the thigh is assumed to be inhomogeneous. Some interesting results can be observed. With the water bolus, a hot spot can be observed in the inhomogeneous thigh case near the top edge of the applicator. This is not present in the case of the homogeneous thigh. Deepening and broadening of the SAR pattern is observed with the bolus compared to the case without the water bolus. Also in the inhomogeneous case, there are number of smaller hot and cold spots present largely due to tissue inhomogeneities.

These results indicate that the SAR patterns measured in planar phantoms can not give a very accurate picture of the SAR patterns in clinical situations where the inhomogeneous tissue structure and shape of the dielectric scatterer markedly influences the patterns. Further, these 2-D results do not take in to account the effect of 3-D variations which may further modify the SAR distributions and work is in progress to investigate these 3-D effects.

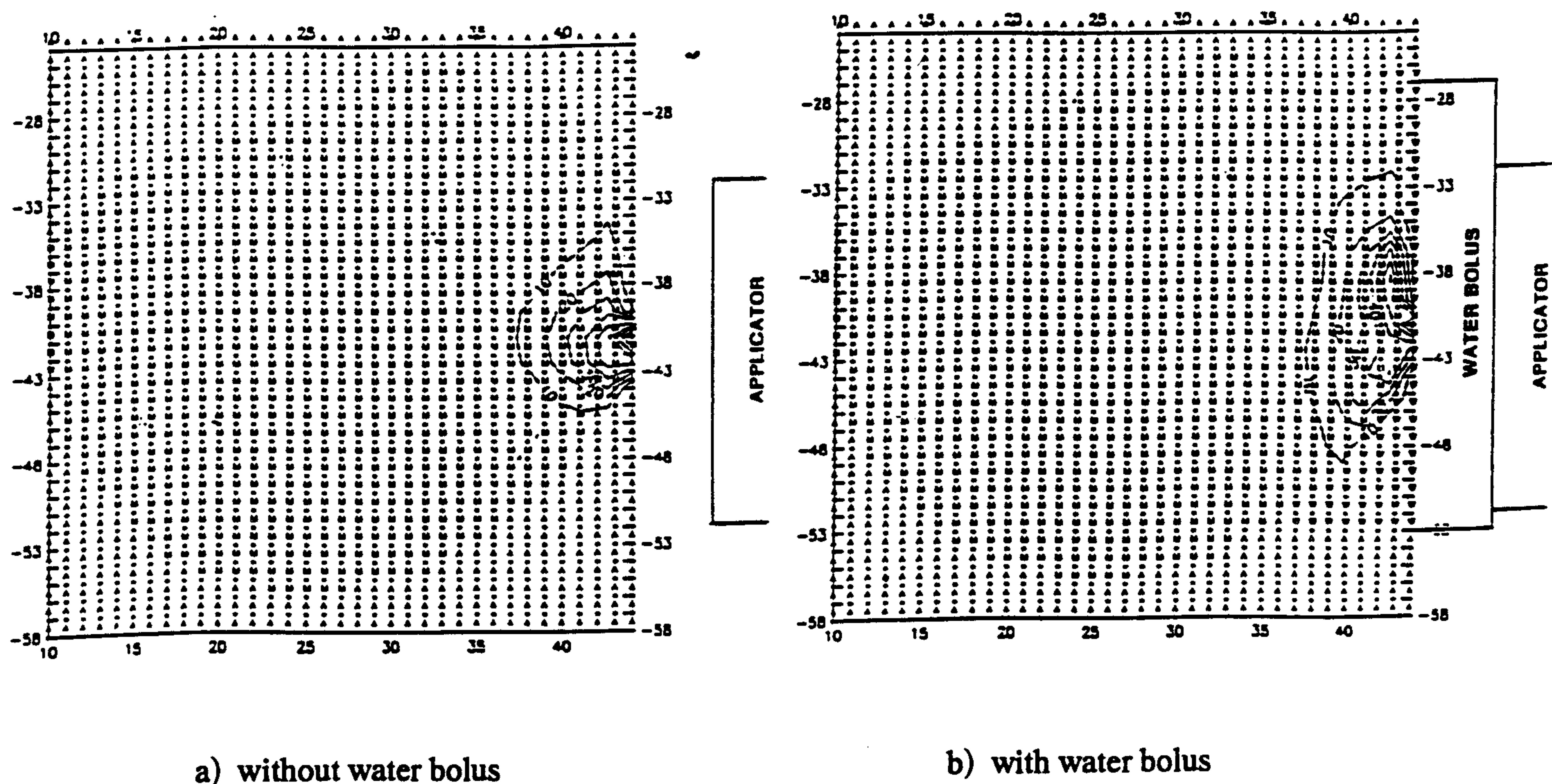


Figure 2. Normalized percent SAR distributions in a homogeneous thigh (M-Muscle, W-Water, A-Air)

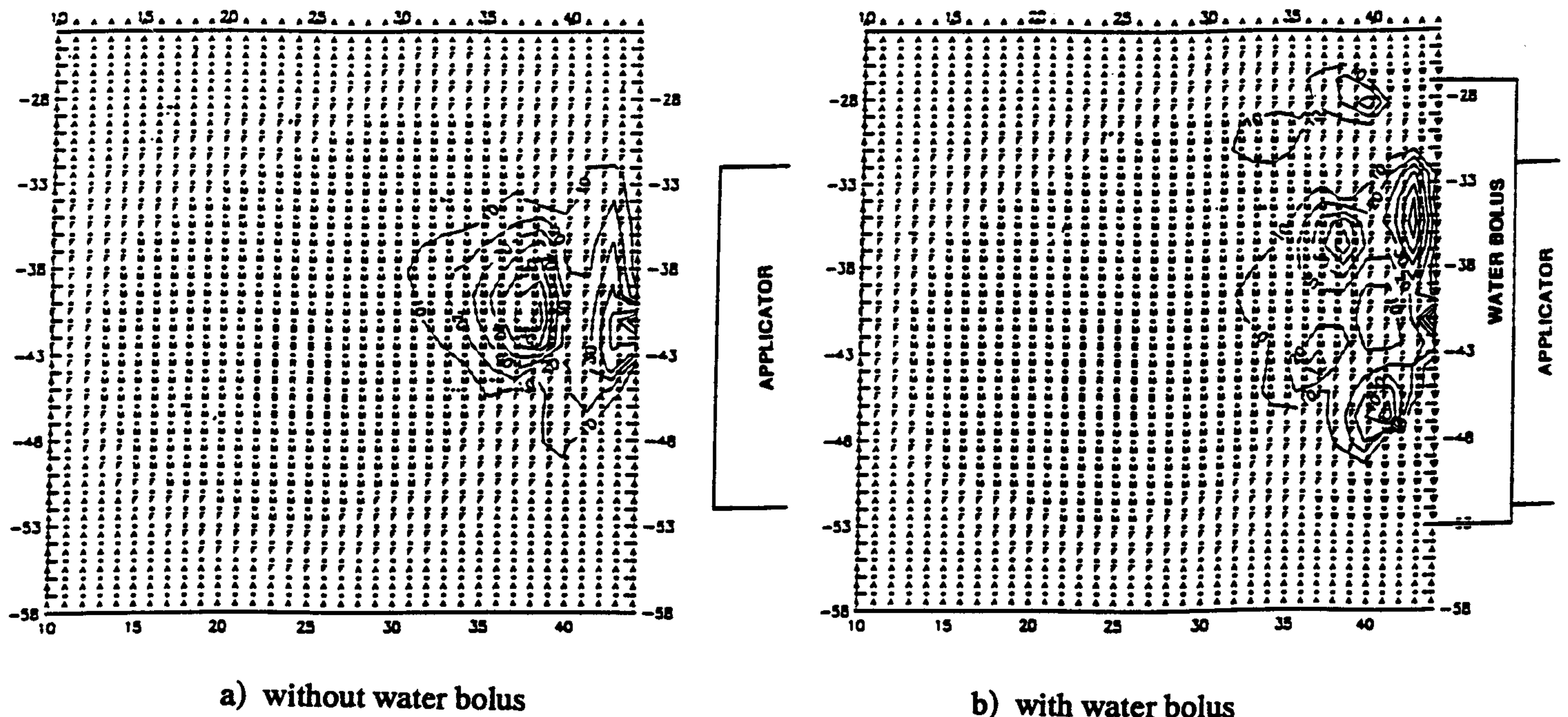


Figure 3. Normalized percent SAR distributions in an inhomogeneous thigh (M-Muscle, F-Fat, B-Bone, R-Bone marrow, W-Water, A-Air)

Future Needs in the EM Modeling Area

The computed SAR distributions for realistic geometries presented above show some interesting features which may not readily be appreciated from planar phantom measurements. Two important issues have to be addressed. First is the question of whether the observed distributions are real or are due to some numerical artifacts. The extensive validations carried out by comparing with MoM results give some confidence in the calculations. Yet it is important to carry out further experimental validations for selected cases before full confidence can be placed on these numerical models. Validation studies will have to consider both applicator free-space operation as well as loading by media having the electrical characteristics of biological tissue.

The second issue is whether the observed SAR hot spots will result in corresponding temperature hot spots. Two distinct modeling problems are involved in the computer simulation of hyperthermia treatments: computation of the absorbed EM power distribution in tissue and the prediction of resulting temperature distributions using a suitable thermal model. These are two complex problems requiring different theoretical basis and tissue property and physiological data. Development of suitable thermal models to predict the resulting temperature distributions is also an active area of research. However, the limited bloodflow data available and the heterogeneous blood flow distribution in tumors may limit the applicability of this approach. There is active research ongoing to obtain bloodflow data using positron emission tomography (PET) systems. Overall, accurate numerical models to calculate power deposition and temperature distributions would be valuable tools to improve the delivery of hyperthermia and thus significantly enhance its role in cancer treatment.

Computer modeling can play a significant role in the design of better heating equipment and in improving the quality of the hyperthermia treatments currently being administered. However, there are several gaps in the state of the existing knowledge regarding the validity of numerical

simulation in the clinical context. There are also a number of important EM field physics issues unique to hyperthermia: 2-D vs. 3-D modeling quantification; analytical and experimental validations; and understanding realistic antenna/patient configurations; that need to be addressed.

It is concluded that FD-TD computational modeling, with stepped-surface approximation of tissue structures, will remain for the near future as the most efficient means of obtaining predictive data for EM field penetration into biological tissue structures in 3-D. Research into time-domain finite-elements, however, may ultimately provide an alternative means of such modeling since the time-domain formulation permits in principle explicit or nearly-explicit time-marching of the fields. This is the key to dimensionally-low computer resources and processing by supercomputers.

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