Evaluation of Clinical Hyperthermia Treatment Using Time Domain Finite Difference Modelling Technique

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Abstract

The use of numerical modelling techniques, especially the time domain finite difference method, has improved the understanding of power deposition in human bodies undergoing cancer treatment with microwave or radio-frequency waves. In this paper, clinical hyperthermia treatments are modelled with the time domain finite difference method. Quantitative assessment criteria are defined for the evaluation of computed power deposition patterns and are found to be useful in determining whether a particular treatment is likely to succeed.

1. Introduction

Microwave or radio-frequency wave induced hyperthermia is a method of treating cancer by raising the temperature of malignant tissues to 42-43°C for an extended period of time. One major concern in electromagnetic hyperthermia is to be able to deposit sufficient amount of power in the cancer tumour sites without overheating other healthy tissues. The human body is a complicated heterogeneous dielectric body and the physics of electromagnetic interactions dictates that the irradiation of such a body will result in highly non-uniform field distribution and heating pattern.

In the past decade, computational electromagnetics has been applied to the design and evaluation of antennae (applicators) used in electromagnetic hyperthermia [Iskander *et al.* 1982; Lau *et al.* 1986; Shaw *et al.* 1991] and the calculation of whole body power absorption of un-intended electromagnetic radiation [Spiegel *et al.* 1989]. Computational electromagnetics has been particularly useful in hyperthermia because of the immense difficulty in monitoring either power or temperature within the patient.

The time domain finite difference (TDFD) method [Taflove and Umashankar, 1989] of solving Maxwell's equations has become widely used in computational electromagnetics in general. This can be observed from the ever increasing number of papers published and presented [Miller, 1991] on this method. It has long been recognised that the TDFD method is well suited for the hyperthermia problem [Lau and Sheppard, 1986] due to its efficiency in the usage of computing resources.

With the potential ability to achieve better localization of power and deeper penetration into the body, the annular phased array (APA) hyperthermia system has been used in many hyperthermia centres over the world. The system is based on the principle of phased antenna array. It is hoped that by varying the phase and amplitude of individual applicators, field pattern can be steered to allow the tumour site to be selectively heated up.

The APA hyperthermia system has been modelled extensively with the TDFD method [Wang and Gandhi, 1989; Sullivan, 1990; Lau and Sheppard, 1990]. Computed data have also been validated by experiments performed on homogeneous tissue-equivalent phantoms [Sullivan, 1990; Sullivan, 1991]. Techniques based on TDFD simulations have been proposed for planning hyperthermia treatment [Sullivan, 1991]. Although simulations have been carried out on patient-specific models (i.e. those constructed from tomographic scans), the computed data have yet to be validated due to experimental difficulties. So far such studies yield valuable information on the performance of the APA system under various applicator placement, phase and amplitude settings. However, little work has been reported on if and how data from computer models can be related directly to real clinical treatments. Such correlation study must be pursued to build up the confidence of clinicians in the use of simulation data, in parallel with other effort such as building better and faster models.

This paper aims to demonstrate how TDFD models can be correlated, albeit in a qualitative manner by necessity, to clinical observations. Quantitative parameters are defined to assess the effectiveness of treatment using an APA hyperthermia system.

2. Method

As the TDFD method has been well documented in many publications [Taflove and Umashankar, 1989], only the briefest account of the algorithm will be given here. Maxwell's two time dependent curl equations are approximated by an explicit finite difference scheme in cartesian coordinates. The E and the H field components are positioned on a lattice first proposed by Yee [Yee, 1966]. Given an initial field excitation, explicit time-marching is performed alternately on E and H field components until steady state is reached. Dielectric and metallic objects are represented by collections of cubic lattice cells which have identical permittivity and permeability values assigned. Details of the code used for this study can be found in [Lau and Sheppard, 1986].

Two dimensional models based on the BSD-1000 hyperthermia system were used in the current study. Figure 1 illustrates a typical model consisting of eight waveguide applicators surrounding the patient. The gap between the apertures of the applicators and the patient was filled with de-ionized water. The patient area of the models was constructed from computer tomographic (CT) images obtained in a plane containing the maximum area of a tumour in the pelvic region. Closed boundaries of all the organs on the CT slice were first digitized manually and the TDFD code filled in each organ with the appropriate dielectric properties automatically. The dielectric parameters used for the models are shown in table 1.

Three field components, namely Ez, Hx and Hy were solved in the models. The waveguide applicators were excited with a sinusoidally varying Ez source across the width of each applicator. The amplitude of the source was modulated by the term $\sin(\pi x/a)$ where a is the width of the waveguide aperture and $0 \leq x \leq a$. The width of each waveguide was 0.2m and the length was 0.15m. The frequency modelled was 60 MHz. The spatial resolution of the uniform finite difference grid used was 0.004m and all models consisted of 200 by 200 lattice cells. The temporal resolution used for the time marching was 0.004m divided by twice the speed light in free space. Steady state $|E|$ field value at each lattice cell of the model was extracted after six cycles of the incident wave had elapsed, the equivalent number of time steps needed for each run was 14988. The power deposition in the patient was also computed at each cell by the specific absorption rate (SAR), defined as: $\sigma|E|^2/\rho$ where σ was the electrical conductivity and ρ was the density of the tissue. The unit for SAR is W/kg.

The computer platform used for the study was a VAXstation 3100 with 24MB main memory running VMS operating system. The TDFD code was written in standard Fortran 77 [Lau and Sheppard, 1986] and the processor time required for each run was on average three hours. The actual memory required for the simulation was about 1.25MB. Graphics pre- and post-processing offered by this TDFD code was based on either the UNIRAS package or the built in window software of the computer.

3. Case Studies

In this section, simulations and clinical studies on three patients are reported. In all the TDFD data computed, two parameters are used to assess the quality or the effectiveness of a treatment. The maximum tumour SAR is simply the maximum value of SAR (in W/kg) found in the tumour. The treatment ratio is defined as ratio of the average SAR in the tumour to that of the nearby sensitive organ. In clinical hyperthermia treatments, it is usual to monitor the tumour and a nearby organ which can easily be damaged by excessive heating. When the temperature in the nearby organ rises above the tumour being treated, the treatment is aborted. Hence the evaluation of treatment ratio as defined parallels the clinical monitoring procedure.

The size of each of the patients was measured in terms of the major and minor axes of the CT image of the patient as illustrated in figure 1. Table 2 shows the dimensions of the three patients reported in this study.

3.1 Patient I

This patient suffered from a rectal tumour and the nearby sensitive organ was chosen to be bladder. When the patient was treated with the BSD-1000 system with all applicators in phase and with equal power, the temperature of the bladder was observed to rise above that of the tumour. The session was aborted and a phase lag of 65° was introduced to half of the applicators (1,2,7 & 8) before treatment resumed. The bladder temperature was seen to drop below the tumour temperature which increased and the treatment was allowed to continue for a further period of time.

Computer simulations were performed on this patient with both the in-phase and the 65° phase lag settings. Figure 2 shows the field distribution in the entire system for the in-phase treatment. The corresponding SAR distribution in the patient is shown in figure 3. The SAR distribution of the 65° phase lag treatment is presented in figure 4.

The maximum tumour SAR's and treatment ratios were calculated for both treatments and are shown in table 3. It can be seen that the improvement in the treatment is reflected by the increased values of both parameters in the 65° phase lag case, especially in the substantial increase in the treatment ratio.

3.2 Patient II

It has been observed clinically that in patients with central pelvic tumours (e.g. bladder tumour), localisation of heating in the tumour is more difficult to achieve than other off-centre tumours such as those presented in Patient I. Generally, the whole body heats up fairly uniformly and treatment is then aborted due to excessive blood pressure and heart rate, both physiological responses to an overall temperature rise in the body.

In order to see if such observation can be made from a computed SAR pattern, a patient with bladder tumour was simulated with all applicators irradiating in-phase. The resulting SAR pattern is shown in figure 5. The nearby sensitive organ for this patient was the rectum. The maximum tumour SAR and the treatment ratio are shown in table 4, they indicate that power absorption in the tumour is low and selective heating is extremely poor. It should also be noted that the maximum tumour SAR in this patient is much lower than that of Patient I, indicating that it would be more difficult to raise the bladder tumour to the desired hyperthermic temperature range compared with patients with rectal tumours.

3.3 Patient III

This patient suffered from a bladder tumour as Patient II. However, the size of this patient was larger than Patient II. The nearby sensitive organ was also rectum.

TDFD simulation was carried out for this patient. The SAR pattern is shown in figure 6 and the assessment parameters for this patient can be found in table 4. The treatment ratio is very similar to that of Patient II but the maximum tumour SAR is lower. These values suggest poor localisation of heating inside the tumour and that it would be more difficult to raise the tumour temperature of a large patient than in a smaller patient. Such trends are again often observed in clinical hyperthermia treatments.

4. Conclusions and Discussions

In this study, it has been shown that by applying quantitative analysis to data obtained from TDFD simulations, clinically relevant information regarding the effectiveness of a treatment can be obtained. Specifically, it has been demonstrated that features obtained from computed data corresponded well to clinical observations in :

(1) the improvement of treatment of rectal tumour when the APA system is operating with a phase shift between groups of applicators;

(2) the difference between treatment of central and non-central tumours; and

(3) the difference between treatment of patient with different sizes.

The three cases presented in this paper are samples from a large number of patients which have been similarly analyzed. Through systematic evaluation and organization of such data, a data base has been constructed. It can provide clinical practitioners of hyperthermia with useful guidelines which they can understand and apply with confidence to the treatment planning and have some idea as to the degree of success they can expect.

The simulation and analysis presented in this work cannot replace rigorous experimental validation through field and temperature measurements in patients or realistic tissue-equivalent phantom. Nevertheless, it provides a practical way to allow data from computer models to be related to clinical experiences.

This work was performed mostly on two dimensional models due to the fact that computing resources required to evaluate a large number of cases in full three dimensions are still prohibitively large. However, a small number of three dimensional TDFD models have been built and data from such simulations so far are consistent with the findings from the two dimensional work.

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Table 1 : Dielectric Properties Used for TDFD Models at 60 MHz

Dielectric	Relative Dielectric Constant	Conductivity (Sm^{-1})
Water at 15°C	82.24	0.001
Bone	7.35	0.053
Fat	15.05	0.215
Muscle	83.85	0.791
Skin	77.27	0.540
Bladder/Tumour/Rectum	87.38	0.750

Table 2 : Dimensions of Patients in Case Studies

	Major Axis (cm)	Minor Axis (cm)
Patient I (female)	32.2	22.5
Patient II (male)	33.1	18.8
Patient III (male)	35.0	24.1

Table 3 : Treatment Assessment for Patient I

	Maximum Tumour SAR (W/kg)	Treatment Ratio
All applicators in phase	11.7	2.81
App. 1,2,7,8 at 65° phase lag	14.5	5.21

Table 4 : Treatment Assessment Comparison for Patients I,II and III (treatment with all applicators in-phase)

Patient	Maximum Tumour SAR (W/kg)	Treatment Ratio
I (rectal tumour)	11.7	2.81
II (bladder tumour)	4.6	1.31
III (bladder tumour)	2.1	1.29

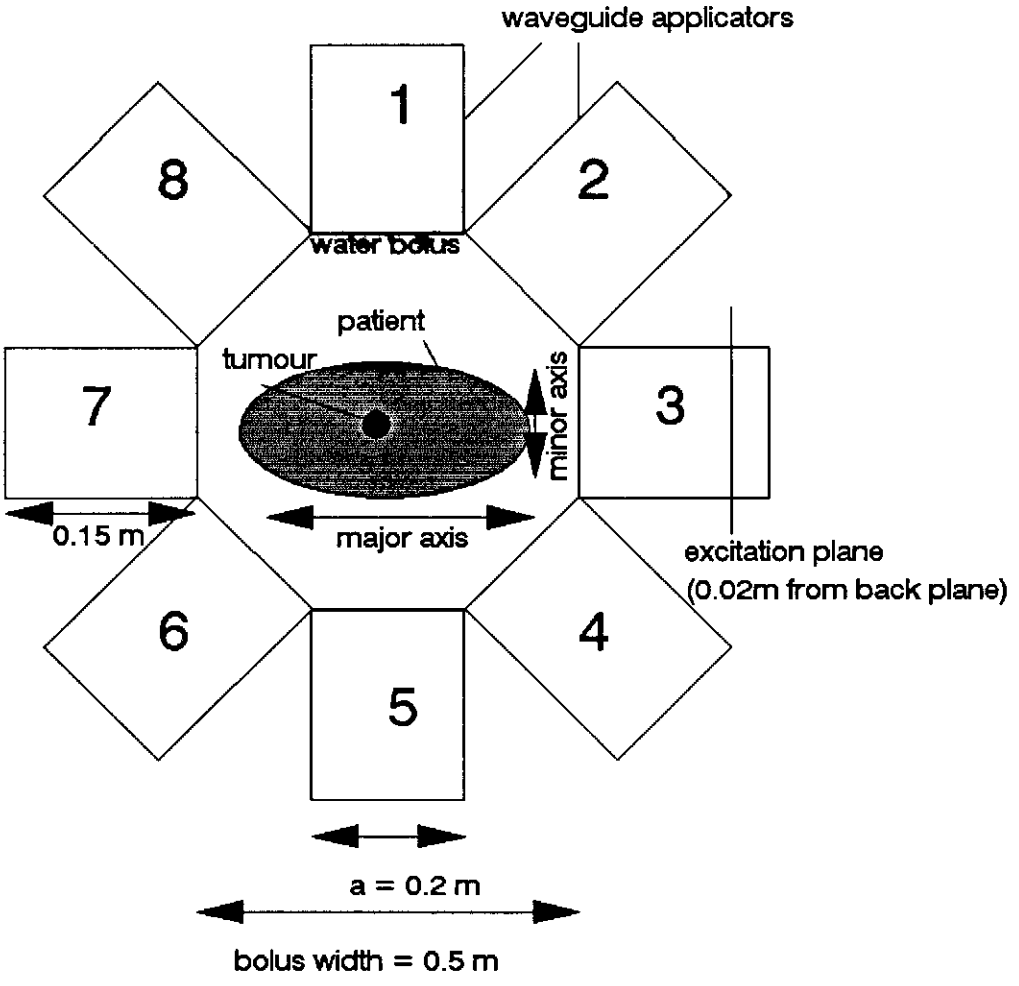

Figure 1 : TDFD Model of APA Hyperthermia System

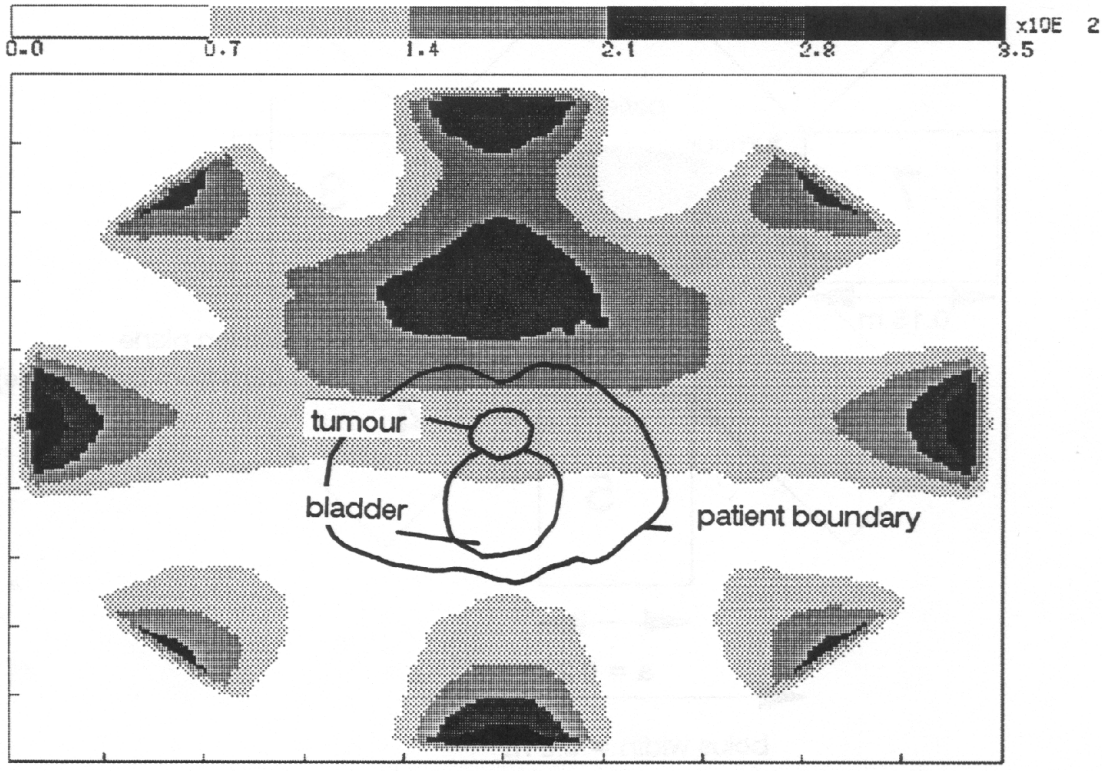

Figure 2 : |E| field plot of model when Patient I is treated with all applicators in-phase. Range of relative field values plotted is 0 - 350 V/m.

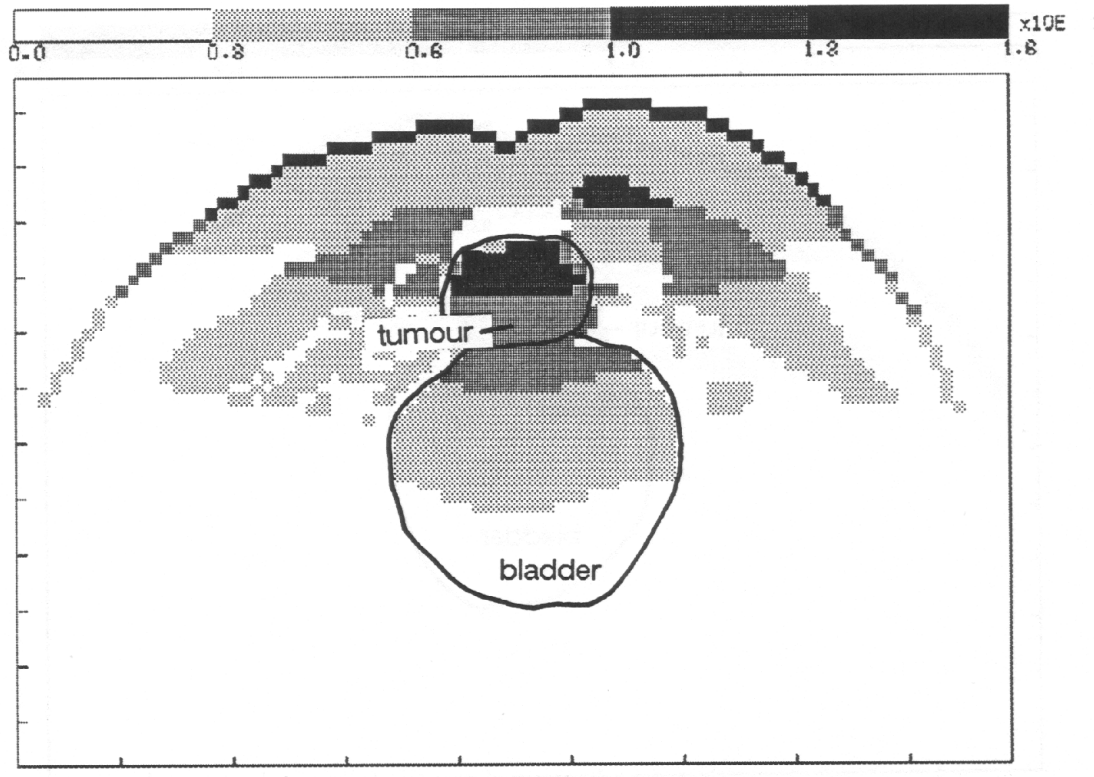

Figure 3 : SAR plot of Patient I when treated with all applicators in-phase.
Range of grey scale displayed corresponds to 0.0 - 16.2 W/kg.
Maximum tumour SAR is 11.7 W/kg.
Physical dimensions plotted is 0.356 m (width) by 0.252 m (height).

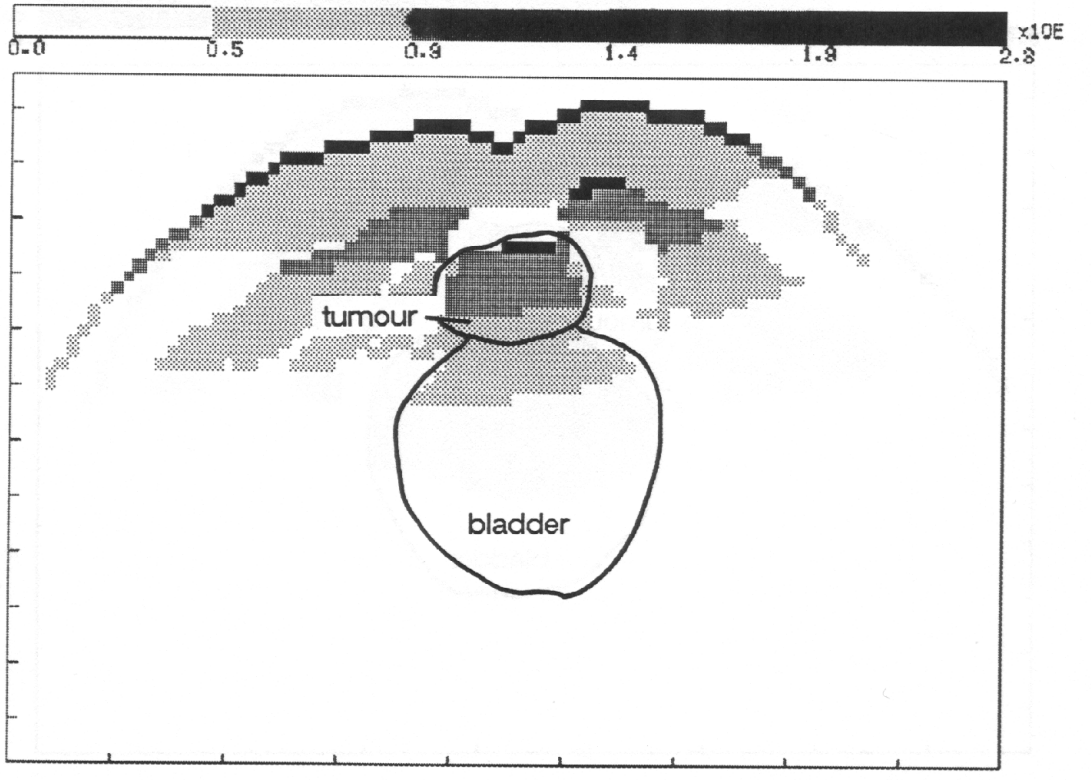

Figure 4 : SAR plot of Patient I when the phase of applicators (1,2,7 & 8) lags the rest of the applicators by 65°.
Range of grey scale displayed corresponds to 0.0 - 23.0 W/kg.
Maximum tumour SAR is 14.5 W/kg.
Physical dimensions plotted is 0.356 m (width) by 0.252 m (height).

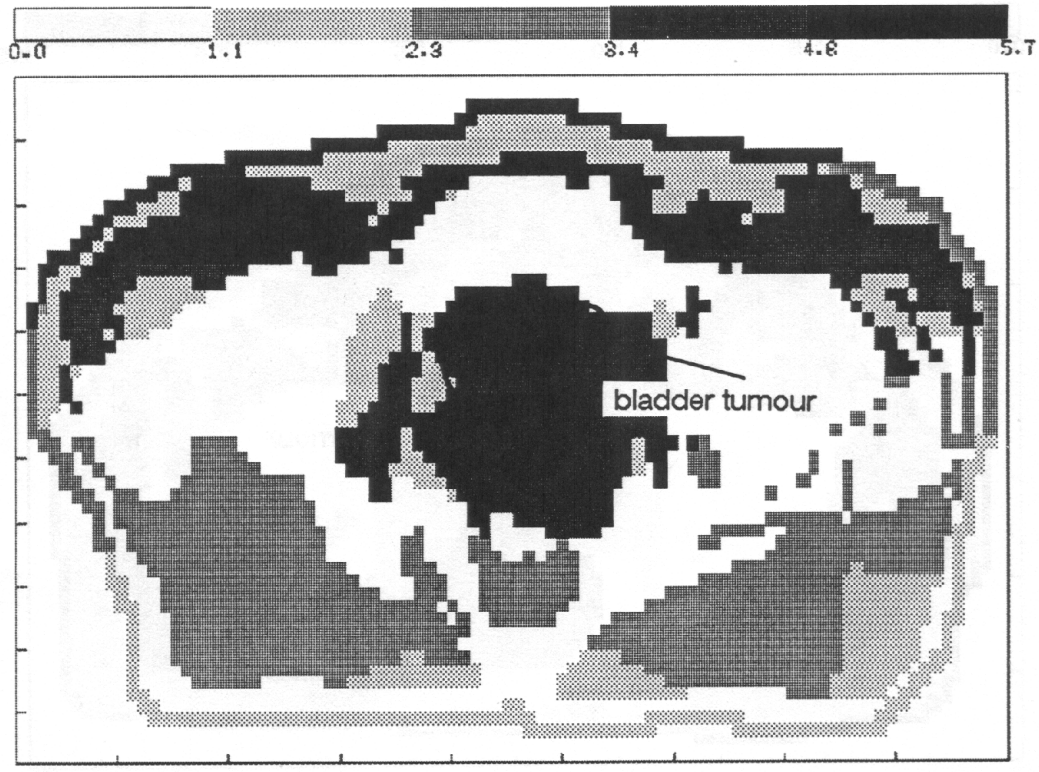

Figure 5 : SAR plot of Patient II when treated with all applicators in-phase.
Range of grey scale displayed corresponds to 0.0 - 5.7 W/kg.
Maximum tumour SAR is 4.6 W/kg.
Physical dimensions plotted is 0.360 m (width) by 0.220 m (height).

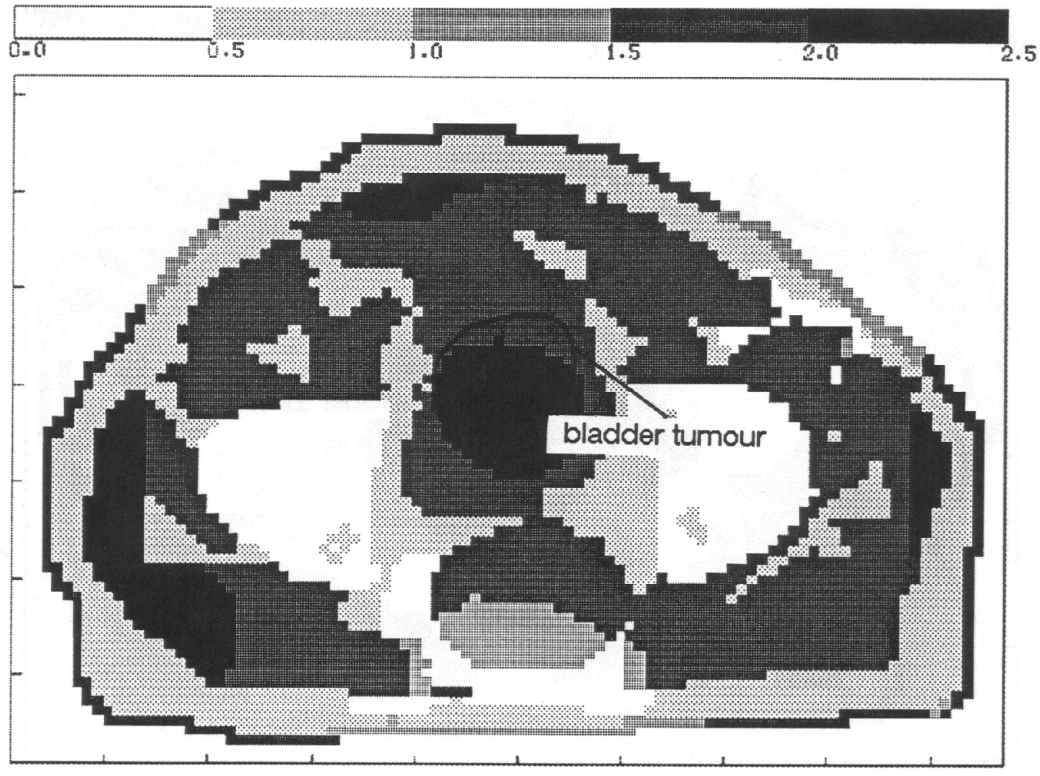

Figure 6 : SAR plot of Patient III when treated with all applicators in-phase.
Range of grey scale displayed corresponds to 0.0 - 2.5 W/kg.
Maximum tumour SAR is 2.1 W/kg.
Physical dimensions plotted is 0.388 m (width) by 0.288 m (height).