Enhanced Energy Localization with Wideband Hyperthermia Treatment System

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Abstract **─** This paper presents a tool to enhance hyperthermia treatment based on multichannel wideband system. The potential of this system in enhancing energy localization is investigated. A model is developed for the hyperthermia treatment plan taking into account cylindrical phantom of human head. Dispersive modeling of tissue properties is used to allow wideband simulation. Problem formulation for optimization of wideband system is presented. Simplified time-delay tool based on coherent phased-array approach is developed and presented. The results reveal the potential of wideband system compared to conventional narrow band systems in enhancement of energy focus. Investigation of advanced optimization processes is introduced that allow real time shaping of the signal waveform in wideband systems. The research addresses the importance of incorporating recent techniques in processing big data to facilitate adopting wideband hyperthermia in clinical systems.

Index Terms **─** Big data, energy localization, hyperthermia treatment, wideband systems.

I. INTRODUCTION

Big data is predicted to contribute considerably in healthcare applications by enhancing the performance at lower cost. Big data is characterized in different dimensions including volume, variety, velocity, and veracity. In biomedical and healthcare domains volume indicates the exponentially growing size of data [1, 2]. As an example the healthcare data is predicted to increase form 500 petabytes in 2012 to 25,000 petabytes by the year 2020 [3]. Variety of biomedical data signifies the heterogeneous nature of data types characterizing patients. The big data revolution is thus shown to accelerate value and innovation in health care [4] .

The tools associated with big data allows the move from population based treatment plans to patient specific treatment plans. Plans can be established to enhance the efficacy and specificity of the treatment by optimizing the system capabilities to the patient. These directions motivated this research to enhance hyperthermia treatment (HT). A multi-channel wideband system is proposed to overcome limitations of conventional systems in energy localization to tumor regions.

Hyperthermia is found to be effective in eradicating cancerous tissues in various regions including breast and head and neck. During hyperthermia, the temperature of malignant tissue is raised to 40-45C° [5, 6]. Hyperthermia reduces the vitality of malignant tissues and increases their sensitivity to radiotherapy and anticancer drugs. Hyperthermia can thus reduce the required doses and the associated side effects of treatment plan.

External HT provides an attractive non-invasive therapeutic plan [7, 8]. The potential of effective treatment however depends on the capability of localizing energy onto tumor regions without affecting the healthy tissues. This requires a high level of precision and accuracy in the treatment planning [9]. With differences in age, size, and tumor locations of patients, success of the treatment plan depends on the development of patient-specific treatment plan derived from patient-model-based data. The technical capabilities of the treatment system should also be enhanced to provide more flexibility and adaptivity in enhancing the energy localization schemes. This research thus aims at enhancing the degrees of freedom available to the system in terms of increasing the number of channels and the operation bandwidth. Computational tools are developed to allow handling of big data associated with patient interaction with energy sources.

II. INVESTIGATION OF WIDEBAND HYPERTHEMRIA SYSTEM

Feasibility of wideband hyperthermia is investigated by building a model of the interaction between tissues and energy sources. A simplified head phantom model is built using CST microwave studio [10], implementing a four-layered cylindrical phantom of radius 10 cm is chosen to represent a human head. The inner 8-cm radius cylinder is used for depicting brain tissue and the outer three cylinders for gray matter, cerebrospinal fluid (CSF)

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and skull of radii of 8.4, 8.9 and 9.4 cm respectively. This model is shown in Fig. 1 (a). The applicator ports are arranged in counter clockwise direction around the phantom shown in Fig. 1 (b). The tumor is chosen to be of spherical shape of radius 2.5 cm, and is located at x = 3 cm, y = 4 cm and z = 0, as shown in Fig. 1 (c), where origin is set at the center of the phantom. For an acceptable compromise of resolution of reconstructed image, penetration of EM signals and the antenna size, a Gaussian pulse of bandwidth (0.3 to 2.5 GHz) is applied to each excitation port as shown in Fig. 1 (d).

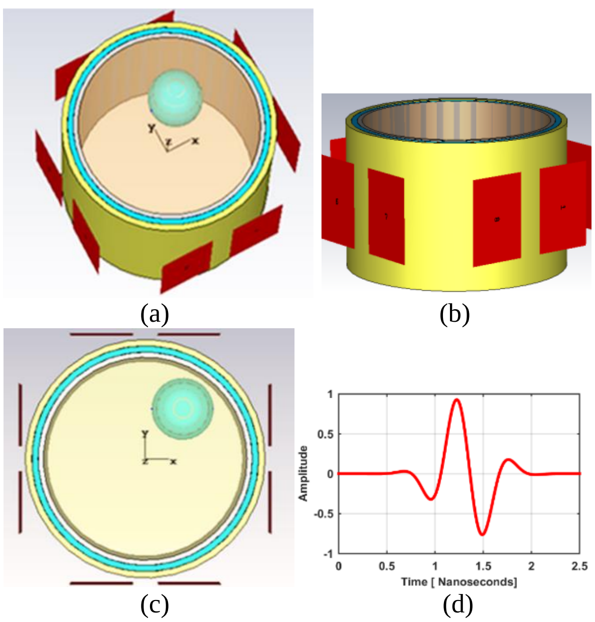


Fig. 1. (a) Perspective view of proposed wideband hyperthermia treatment, (b) side view of proposed model to indicate arrangement of ports, (c) front view of proposed model to indicate the location of tumor, and (d) wideband excitation signal.

The big data characteristics of our proposed model are discussed below.

A. Volume of system

The model consists of multi-channels under wideband excitation to heat a certain sensitive tissue region. Eight channels are shown in this simulation for treatment of brain tumors. This model presents complexity in various dimensions. The first dimension is the bandwidth of operation. Multichannel wideband treatment allows treatment of both superficial as well as deep-seated tumors with appropriate spatial resolution. Optimization of excitation waveform at each port is essential to allow energy localization. The waveform can be modeled as excitation of a number of subcarriers. Each subcarrier is optimized for magnitude and phase. In addition, the problem depends on tumor data. The number of tumors and the size and location of each tumor contribute to the volume of data associated with this problem.

B. Veracity of system

The second dimension is the accurate modeling of human head tissue. The heterogeneous nature of human head representing different tissues levels such as brain, gray matter, cerebrospinal fluid (CSF) and skull along with tissue characterization of tumor in terms of its location, shape and size need to be modeled accurately under a wideband excitation signal. This makes the veracity of our problem. For this purpose, the dispersive dielectric properties of brain tissue and tumor are chosen in accordance with [11-13] and are shown in Figs. 2 (a) and (b).

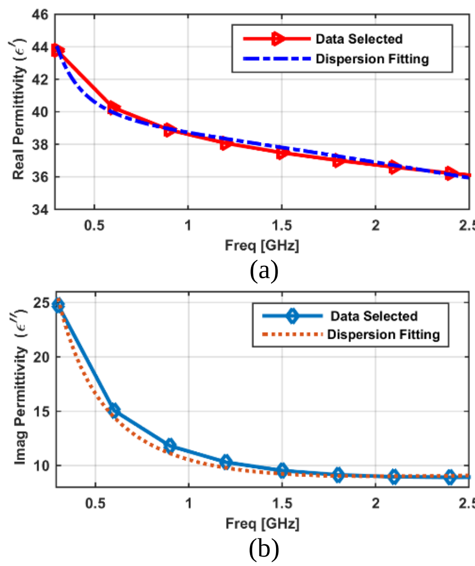


Fig. 2. Behavior of human brain tissue in terms of permittivity under wideband excitation for: (a) real permittivity and (b) imaginary permittivity values.

C. Variety of system

The third and important dimension of the undertaken case study is the variety of the problem as we are analyzing the problem in two different domains under different simulations environment thus making the validation of the problem indispensable. For this purpose, we devised a time-delay tool to focus energy at cancerous region. This tool is incorporated in both configurations to investigate the equivalency of transformation process while shifting from model-to-data transformed configuration.

D. Velocity of system

With the increase of number of channels of the system and the number of subcarriers in each channel, the number of degrees of freedom becomes high and the optimization process becomes computationally complex. Devising an appropriate optimization tool can lead to minimum utilization of system resources and expediting treatment process. Theoretically, an appropriate problem formulation can lead to effective optimization. For this reason, we investigate the optimization problem in different scenarios as follows.

III. OPTIMIZATION PROBLEM

Advanced optimization with the aim to achieve an effective optimization, several techniques have been reported in recent research particularly in the domain of wideband. Three-dimensional time reversal technique in hyperthermia treatment to accumulate energy in head and neck tumors [14]. The waveform transmitting diversity approach for wideband MIMO radar [15, 16] can be implemented to enhance energy localization in hyperthermia treatment. Beamforming methods can also help the implementation of energy localization. It includes non-uniform and short inverse FFT based wideband beamforming method presented in [17]. Compress sensing beamforming proposed in [18] and sparse array based wideband beamforming discussed in [19]. For speed and flexibility a refined eigen value optimization is adopted in [20].

The optimization of model can be formulated in two scenarios: narrowband and wideband.

A. Narrowband case

Assume that an array of M applicators is located in a coupling or cooling medium surrounding the head region at locations $\mathbf{r}_m (m = 1,2, \ldots, M)$ as shown in Fig. 1 (a). Let $\mathbf{x}_m(n)$ $(n = 1,2, \ldots, N)$ represent the discrete-time baseband signal transmitted by the m^{th} applicator. The baseband signal at a location r inside the head can be described as:

$$y(r,n) = \sum_{m=1}^{M} \Psi(f_0,\ \mathbf{r}_m, \mathbf{r})\, \mathbf{x}_m(n), \tag{1}$$

where f_0 is the baseband frequency and $y(r,n) = \Psi(f_0, \boldsymbol{r}_m, \boldsymbol{r})$ is the tissue interaction function that accounts of propagation attenuation of the electromagnetic (EM) signal inside tissue along with the corresponding phase delay due to the travelling of energy.

Let $\mathbf{a}(\mathbf{r})$ be the transpose of steering vector such that:

$$\mathbf{a}(\mathbf{r}) = [\Psi^*(f_0, \boldsymbol{r}_1, \boldsymbol{r}), \Psi^*(f_0, \boldsymbol{r}_1, \boldsymbol{r}), \ldots \Psi^*(f_0, \boldsymbol{r}_1, \boldsymbol{r})]^{\boldsymbol{T}}, \tag{2}$$

while,

$$\mathrm{X}(n) = [\mathbf{x}_1(n)\ \ \mathbf{x_2}(n)\ \ \ldots\ \mathbf{x}_M(n)]^T, \tag{3}$$

represents the transmitted signal. Equation (1) can be written as:

$$Y(\mathbf{r}, n) = \mathbf{a}^*(\mathbf{r})\mathrm{X}(n). \tag{4}$$

The beam pattern representing the signal power at locations $\mathbf{r}$ and is given by:

$$P(r) = E\{Y(r,n)Y^*(r,n)\} = \mathbf{a}^*(\mathbf{r})\ R\ \mathbf{a}(\mathbf{r}), \tag{5}$$

where $(\cdot)^*$ represents conjugate transpose and E the expectation respectively. R is the covariance matrix of $x(n)$ denoted by:

$$R = E\{\mathrm{X}(n)\mathrm{X}^*(r,n)\}. \tag{6}$$

From Equation (6) it is noted that transmitting beam pattern is a function of target location only. Under the constraint that power form the applicator elements is uniform, we reach at an optimization problem as:
Maximize the function,

$$\xi = \frac{P_i}{P_o}. \tag{7}$$

Subject to,

$$a^*(r)\ a(r) = 1. \tag{8}$$

P_i and P_o represent the spatial integration of absorbed power inside and outside the intended tumor location, respectively.

B. Wideband case

Now consider the case when f_0 is the baseband frequency in the interval $\left[-\frac{B}{2}, \frac{B}{2}\right]$. In such a case we can take the Fourier transform of Equation (1) to get:

$$y(r, \mathrm{n}, f) = \sum_{m=1}^{M} \Psi(f_0,\ \mathbf{r}_m, \mathbf{r})\, \mathbf{x}_m(n, f). \tag{9}$$

The beam pattern at a location r and frequency $(f_0 + f)$ can be written as:

$$P(r, f_0 + f) = |Y(r,n,f)|^2 = |a^*(r,f)\ Y(r,n,f)|^2, \tag{10}$$

where $f \in \left[-\frac{B}{2}, \frac{B}{2}\right]$.

In this case optimization problem is conducted in terms of maximization of ξ such that,

$$\xi = \int_{-B/2}^{B/2} \frac{P_i(f)}{P_o(f)} df. \tag{11}$$

P_i (f) and P_o (f) represent the spatial integration of absorbed power inside and outside the intended tumor location, respectively for a given band of frequencies.

Wideband excitation thus offers higher degree of computational complexity than its counterpart narrowband. Initial investigation is introduced of this optimization problem based on simplified optimization tool, which utilizes the phase shifting characteristics of transmission line model. This tool utilizes the information from the model to focus energy at sensitive region making it able to operate as an off-line standalone module even though the actual model and data are inaccessible. This signifies one of the important big data characteristics known as model-to-data and data-to-information transformation of our undertaken case study.

IV. DATA ANALYTICS

In order to investigate different aspects of our proposed case study a model-to-data based approach is adopted as shown in Fig. 3.

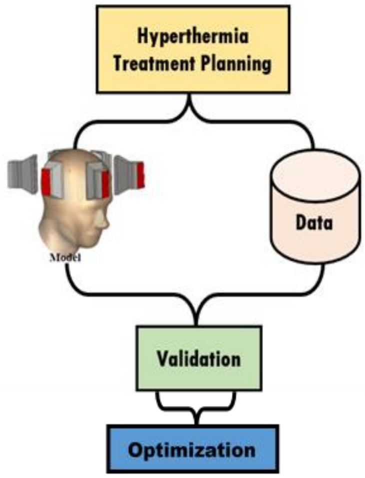


Fig. 3. A model-to-data validation and optimization for wideband HT system.

The data analytics for the proposed case study is divided into three steps as shown in Fig. 4. In the first step patient modeling is done in time domain by choosing appropriate tissue properties of human head and excitation ports using CST microwave studio [10].

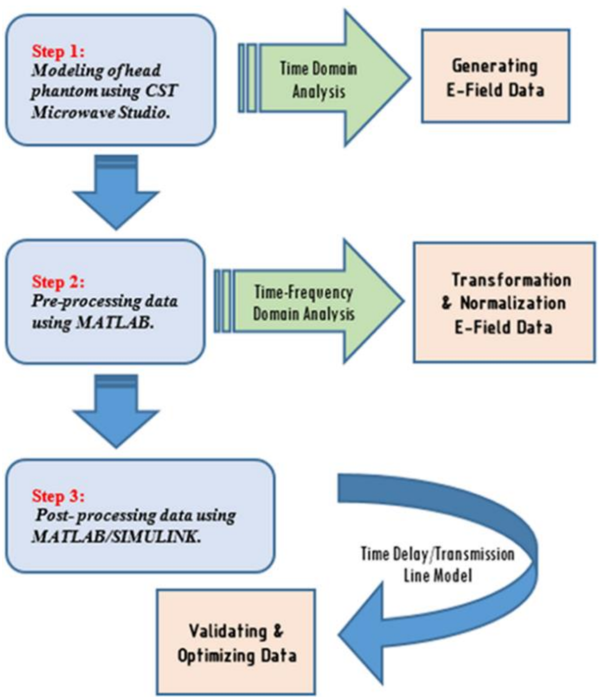


Fig. 4. Flow chart of big data analytics for wideband HT system.

In the second step, this model is transformed to data for pre-processing. The data is analyzed in time and frequency domains and results are visualized in the form of E-field mapping. In the third step, validation of model-to-data transition is achieved using a time delay tool based on coherent phased-array concept. Additionally, an optimization technique using transmission line model is proposed using MATLAB/ SIMULINK. The subsequent sections explain the procedures and techniques adopted in each step.

A. Generating E-field data

As a first step, electromagnetic (EM) simulation of the model shown in Fig. 1 (a) is performed using CST microwave studio. The solver discretizes the model. Time domain field monitors are placed to acquire the E-field data inside the head phantom in three planes as shown in Figs. 5 (a), (b), and (c), covering the tumor in x, y and z directions respectively.

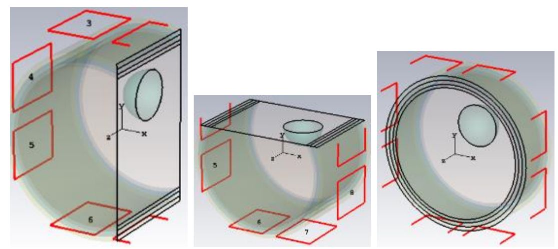


Fig. 5. Representation of proposed model in three normal planes traversing tumor region: (a) x-plane, (b) y-plane, and (c) z-plane.

To reduce the simulation run, the processor hardware is extended with graphical processing unit (GPU) C2070 from NVIDIA, Tesla. With this GPU configuration, the solver took about an hour to complete a run for a total number of 4.63344e6 mesh cells. The time domain E-field data corresponding to these three normal planes is arranged for processing in the next step.

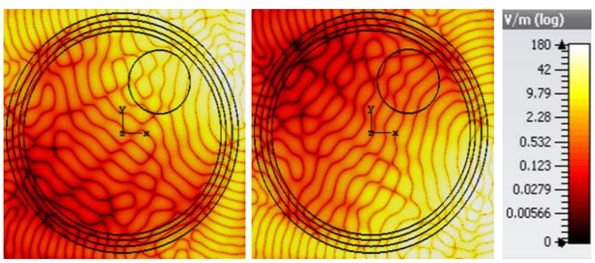
B. Transformation and normalization of E-field data

The time domain E-field data from step 1 is imported to a MATLAB [21] environment for pre-processing. The objective of this model-to-data transformation is to investigate the time-frequency behavior of the model. Additionally, it would allow us more degrees of freedom in terms of processing, organizing, and analyzing the data according to treatment requirement.

The size of each E-field data for a single port in one normal plane is 485 Megabytes (MB). Since we have 8-ports and 3-normal planes, the size of time domain E-field data becomes 485*8*3 (MB). This data is transformed to frequency domain using 256-points FFT. Since the excitation signal is a Gaussian pulse, the frequency domain data is normalized to excitation signal.

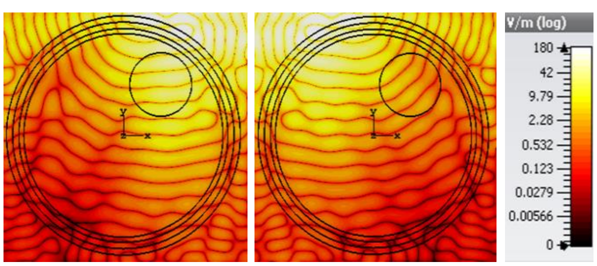
With this data available both in time and frequency domain, it was necessitated to structure the data to be able to use for a variety of requirements. It can be used for narrowband and wideband hyperthermia treatment, for a single and multiple port heating, for superficial and deep-seated HT. The structuring of data in this step allows us to choose any frequency from the available excitation signal (0.3-2.5 GHz) capable to heat the tumor from any port location. As an example, the E-field maps of ports excited with different subcarriers are exhibited in Fig. 6 to Fig. 9.

Figure 6 depicts propagation of E-field when ports 1 and 8 are excited with 2 GHz. Figure 7 shows E-field, when ports 2 and 3 are excited with 1.5 GHz. Results corresponding to exciting ports 4 and 5with frequency of 1 GHz is depicted in Fig. 8. Since ports 6 and 7 are distant apart from tumor location, we choose low excitation frequency such as 0.5 GHz for improved penetration depth. E-field inside the phantom is illustrated in Fig. 9.



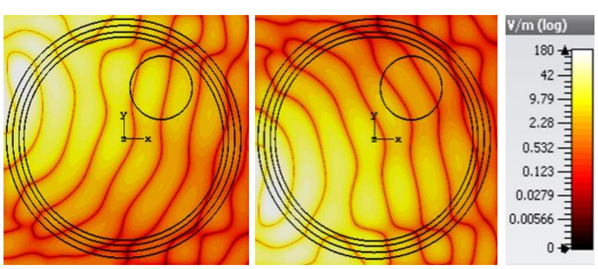
(a) (b)

Fig. 6. E-field map of: (a) port 1 and (b) port 8 excited with 2 GHz.



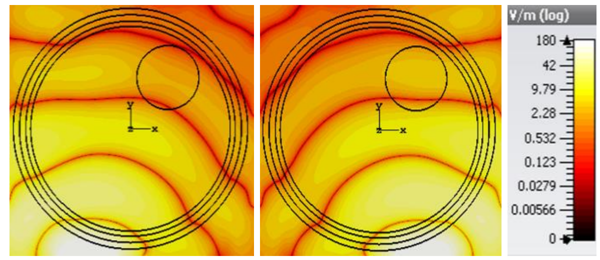
(a) (b)

Fig. 7. E-field map of: (a) port 2 and (b) port 3 excited with 1.5 GHz.



(a) (b)

Fig. 8. E-field map of: (a) port 4 and (b) port 5 excited with 1 GHz.

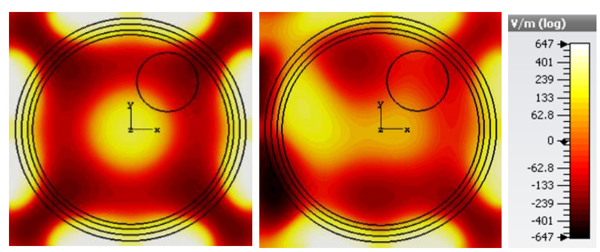


(a) (b)

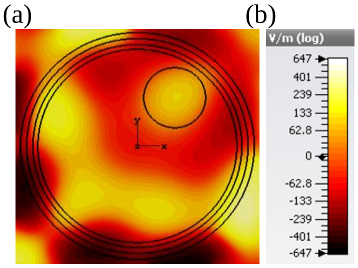
Fig. 9. E-field map of: (a) port 6 and (b) port 7 excited with 0.5 GHz.

C. Validating E-field data

With the objective to guide energy from ports to tumor location, a time delay tool is developed based on coherent phased-array concept [22]. This time delay tool takes all factors into consideration, which makes accumulation of EM energy at tumor region possible with minimum damage to the surrounding healthy tissue. These factors include the phase, amplitude, number of subcarriers, and the propagated distances of subcarriers from the ports to the target region. This time delay tool when implemented in the model-based configuration with different phase shifts gives energy localization at different phantom locations. For a zero phase shift, energy is concentrated at phantom center presenting an ideal case for a tumor to be located at phantom center. In case of an undesirable phase shift, energy is distributed at some off-target region. For a desirable phase shift, maximum energy is focused at tumor location. This is shown by Ez-field map of Figs. 10 (a), (b) and (c) respectively.



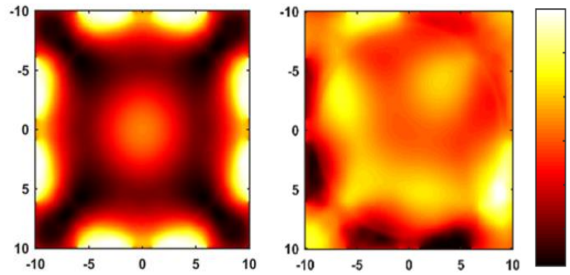
(a) (b)



(c)

Fig. 10. The capability of time delay tool to localize energy. E-field map with: (a) zero phase shift, (b) inappropriate phase shift, and (c) appropriate phase shift when implemented in model-based format.

The time delay tool is incorporated in model-to-data transformed format. The results are show in Figs. 11 (a) and (b), illustrating the potential of this tool in energy localization.



(a) (b)

Fig. 11. The capability of time delay tool to localize energy. E-field map with: (a) zero phase shift and (b) appropriate phase shift when implemented in model-to-data transformed format.

D. Optimization of E-field data

The proposed simplified optimization tool in this research is based on transmission line theory. Transmission line with different shapes and types find a variety of applications in imaging, communication, and high frequency circuit designs. Recently, it is used in real time through wall imaging and for addressing cochlear nonlinearity in acoustic signal processing by utilizing its length and characteristic impedance [23, 24]. For high frequency applications, the length of transmission line (TL) becomes crucial. The phase delays and reflections in transmission line becomes essential to analyze if its length becomes greater than a significant portion of wavelength of the transmitted frequency. The length and characteristics impedance of a transmission line can be related as [25]:

$$V_1(t) - I_1(t) \times Z_0 = V_2(t-\tau) + I_2(t-\tau) \times Z_0, \quad (12)$$

and

$$V_2(t) - I_2(t) \times Z_0 = V_1(t-\tau) + I_1(t-\tau) \times Z_0, \quad (13)$$

where, V_1 is the voltage and I_1 is the current at the source end of the TL, while V_2 and I_2 is the time delayed voltage and current respectively at the load end and τ is the time delay offered by TL. The characteristics impedance of the TL is given by Z_0. The proposed TL model is developed in SIMULINK[21] environment .

The source of TL is connected to carrier and load end is terminated with 50 ohms resistance. A set of four subcarriers with frequency values of 0.5, 1, 1.5, and 2 GHz are considered at each of the eight ports. A tool is developed to adjust the delay of the TL corresponding to each subcarrier to achieve constructive interference at target region and destructive interference away from the target thereby enhancing energy localization. The average power deposition is calculated at each pixel of the phantom, where the phantom is discretized to 80x80 pixels.

With the tumor located at the top-right the results of optimization tool for narrow and wideband hyperthermia are shown in Figs. 12 and 13 respectively. These results demonstrate that the proposed optimization tool accomplishes two objectives. It can be invoked to enhance energy localization at target region and can be used to compare the performance of wideband HT system to the conventional narrowband HT system in terms of energy localization.

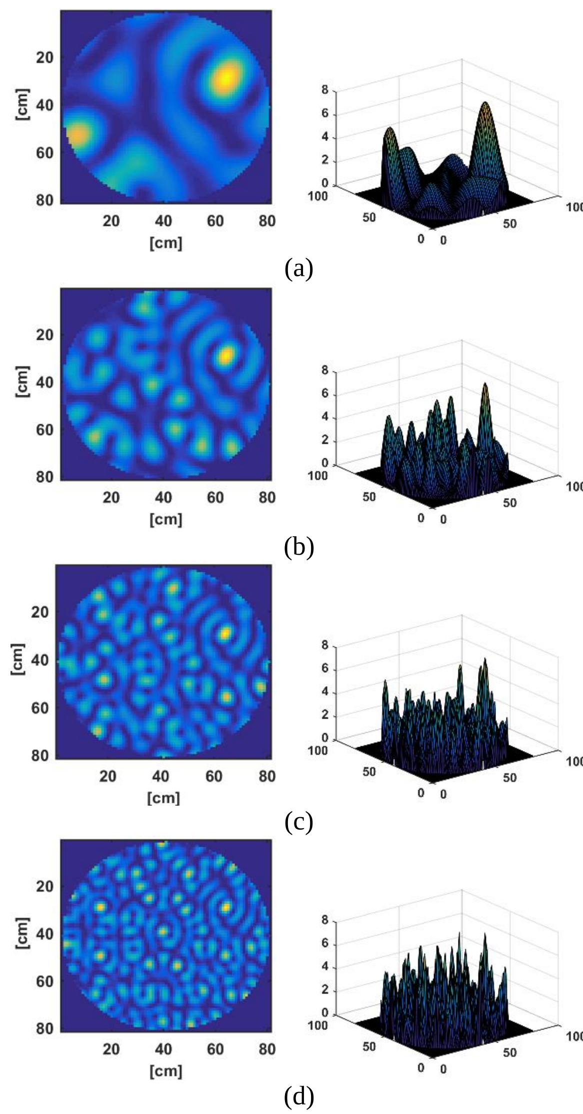


Fig. 12. Energy localization (left column) and corresponding heating pattern (right column) in crucial region for narrowband case: (a) 0.5 GHz, (b) 1 GHz, (c) 1.5 GHz, and (d) 2 GHz.

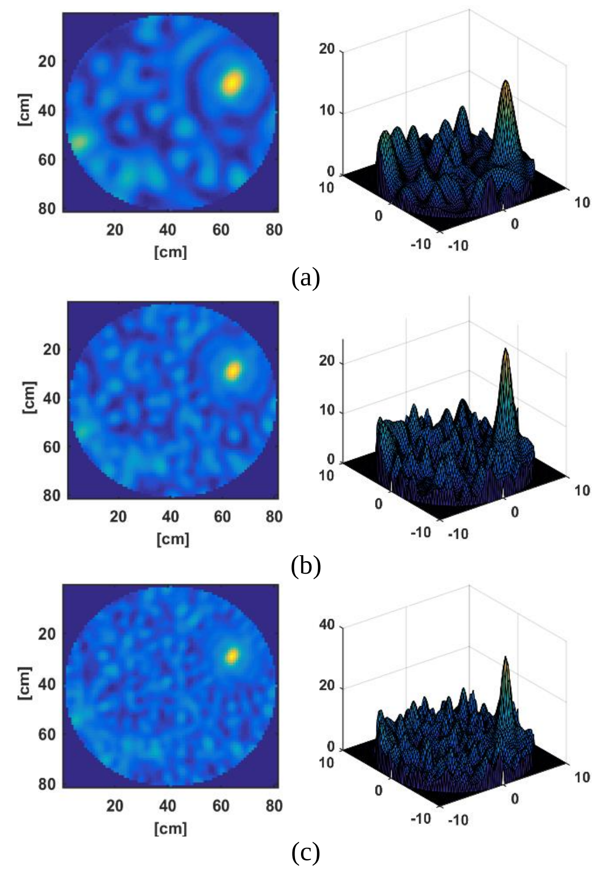


Fig. 13. Energy localization (left column) and corresponding heating pattern (right column) in crucial region for wideband case when: (a) two frequencies (0.5 and 1 GHz) are combined, (b) three frequencies (0.5, 1 and 1.5 GHz) are combined, and (c) four frequencies (0.5, 1, 1.5 and 2 GHz).

V. DISUSSION AND CONCLUSIONS

The potential of wideband system in enhancing hyperthermia treatment is investigated. Mathematical formulation of optimization process is developed to allow energy focus to tumor location, while persevering healthy tissue. Time delay tool is developed and deployed to validate the potential of wideband techniques in energy localization.

The proposed system provides increase in degrees of freedom that allows performance enhancement. Wideband energy can be shaped to target tumors at different depth. Multichannel configuration allows enhancement in energy focus. Model based optimization allows adopting patient-specific model in localizing the energy.

These features however are associated with the need to deal with big data. Clinical adopting of such system will require the development of real time optimization systems that can accommodate various parameters of the system. The tissue properties will also vary within the treatment session in accordance with temperature maps. This requires the update of patient model progressively during the treatment session.

These challenges can be addressed using two approaches. First, the computational capability can be enhanced by adopting cluster techniques. Hardware acceleration has also been used in this research and is found to have real impact on reducing computational analysis time. On the other hand, more robust optimization techniques can be adopted to allow real time use of the optimization tools

This research addressed the use of transformation from time to frequency domain, which allows the efficient handling of big data associated with this problem. Further investigation will consider various signal decomposition techniques. Time reversal techniques should simplify the optimization process by providing an initial solution that can approach close to the global optimum parameter values.

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