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Regularized Nakagami Ultrasound Imaging for Microwave Hyperthermia monitoring

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***Abstract*—The study involves development of ultrasound-based regularized Nakagami imaging (RNI) that improves the quality of Nakagami image. The feasibility of RNI to image the spatial and temporal evolution of hotspot during microwave (MW) hyperthermia experiment was explored on in-vitro polyacrylamide gel (PAG)-agar based phantoms. The normalized cumulative differential regularized Nakagami (NCDRN) maps were estimated from the envelope of beamformed ultrasound radiofrequency (RF) data using proposed RNI technique. The NCDRN maps were estimated at different time instants for the entire duration of the experiment. The experiments were carried out on phantoms at power level of 12 W fed to the microwave antenna. The contour maps of the NCDRN and the ground truth temperature map, obtained using an infra-red (IR) thermal camera corresponding to ultrasound imaging plane, showed that NCDRN was able to locate the axial and lateral co-ordinates of the hotspot with an error of < 1.5 mm axially and < 0.4 mm laterally. This preliminary *in-vitro* study demonstrates that NCDRN maps estimated using the regularized Nakagami imaging may have potential in imaging and evaluating the spatio-temporal evolution of hotspot and may help in the development of ultrasound-based image guided hotspot monitoring system for microwave hyperthermia.**

Keywords—Alternating direction method of multipliers, Microwave Hyperthermia, Nakagami Imaging and Ultrasound Imaging.

I. INTRODUCTION

Thermal treatments for breast cancer can be broadly divided in two major categories such as complete tumor ablation [1] and localized hyperthermia. The hyperthermia is used in tandem with radiotherapy [2] or chemotherapy. The outcome of increased temperature in the localized region of tumor can have drastic effects [3]. A critical sub-system for the microwave (MW) hyperthermia treatment is temperature monitoring, aimed to ensure and confirm that healthy tissues remain safe and that a sufficient amount of thermal dose is applied and delivered to the target tumor. The use of invasive temperature sensors such as thermocouples and fiber optic probes have demonstrated their capability to provide accurate measurement of temperature and thus are used widely in clinical practice. The major downside of this approach is extremely poor spatial resolution due to less number of discrete locations, where measurements can be made. Image-guided thermal monitoring on the other hand is beneficial due to its non-invasive nature and better spatial resolution. Non-invasive nature of the Magnetic resonance imaging (MRI) thermometry coupled with its ability to provide a temperature map, which may be presented as a colored image overlaid on top of the anatomical image. This method is quantitative and offers good temporal resolution. It also covers a wide temperature range [4]. Nevertheless, the major disadvantage of MRI is comparatively expensive, limited accessibility in clinical settings, and further it needs MRI compatible ferromagnetic-free microwave applicators [5]. X-ray computed tomography (CT) based treatment monitoring provides both high temporal and spatial resolution. However it provides relatively low temperature resolution [6], and in addition exposes a patient to a dose of harmful ionizing radiations [7]. Ultrasound (US) is portable, widely available in the clinics, relatively affordable and is capable of providing real-time imaging. Consequently, various research efforts are being under taken recently to harness its potential for thermal therapy monitoring. Investigated methods include B-mode echogenecity analysis, local harmonic motion, shear wave thermometry, thermal imaging and Nakagami imaging to name a few [8]. Additional and elaborate information pertaining to various ultrasound-based approaches can be found in the published review outlined in the reference [6]. Thermometry can also be performed by utilizing the temperature dependence of speed of sound (SOS), which has been quantified and characterized for numerous tissues [9]. The SOS based methods have proved their capabilities to perform well in US temperature monitoring, when temperature is below 50°C.

In this work, we propose a novel method that improvises on the existing method based on the Nakagami parameter imaging. To the best of our knowledge no previous studies have explored the use of the regularized Nakagami imaging (RNI).Therefore, the objectives of this study are to develop a regularized Nakagami parameter estimation and evaluate its performance in monitoring microwave hyperthermia treatment on *in-vitro* phantoms.

II. METHODS

A. Microwave hyperthermia setup

The microwave hyperthermia experimental set-up consisted of a cavity-backed antenna with a C-type radiating patch. The operating frequency was set at 434 MHz [10].A single channel hyperthermia treatment delivery system was used to perform heating experiment. The main sub-systems of the power generation module of MW hyperthermia include RF signal generator (SSG 6000 RC, Mini-Circuits, USA), isolator (JPSS Technologies, India), RF-power amplifier (A150,LCF Enterprises, USA), circulator (JPSS Technologies ,India) and power meter (4304A, Bird Technologies, USA).The temperature of water-bolus was maintained at 32 ℃, by allowing a continuous flow of temperature controlled de-ionized water with the help of a system consisting of a water bath (Equibath, Equitron Medica Pvt.Ltd, India) and a peristaltic pump (RH-P110S-01, Ravel, India). The amplifier remained off for initial 10 min, and then the antenna was excited with forward power of 12 W for the following 20 min. This was followed by a cooling phase that lasted for next 10 min. The reflected power was frequently monitored during the course of experiment and was found to be less than 5 %. The block diagram of the experimental setup is illustrated in Fig.1.

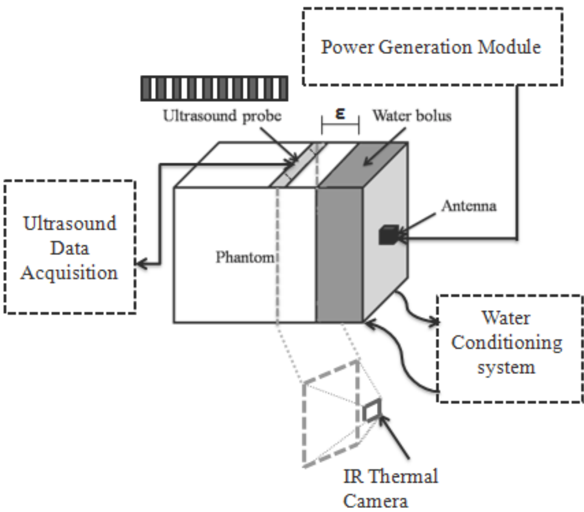

Fig. 1. The schematic depicting the experimental set-up of ultrasound-guided microwave hyperthermia experiment.

B. Phantom preparation and Experiment

Polyacrylamide. (PAG) phantom recipe delineated for hyperthermia application in [11] was used in this study. The phantom was made to resemble a human muscle tissue possessing dielectric properties ($\epsilon_r = 56, \sigma = 0.6$ S/m). A 2 % (weight/volume) agar powder (SRL Pvt. Ltd., India), which acted as ultrasound scatterer was uniformly mixed in solution of acrylamide monomer. For this experiment, a PAG phantom having dimension of a 70 × 70 ×70 mm^3 was created and was heated by the hyperthermia applicator (Fig. 1). During this time raw ultrasound RF data were acquired (details in Section C) and then processed offline. At the end of the heating, the *in-vitro* phantom was sliced along the plane corresponding to ultrasound imaging plane. To capture the spatial distribution of temperature an IR thermal camera (Ti125, FLUKE, USA) was used, which provided the reference ground truth.

C. Ultrasound Data Acquisition

Conventional linear-array focused ultrasound imaging sequence was used in this study. The raw RF data were acquired using the Vantage 64 (Verasonics, Inc. Kirkland, WA, USA) ultrasound scanner. The L11-5v, linear array transducer was used to perform ultrasound imaging. The ultrasound scan parameters used in experiments are shown in Table 1.

TABLE I. ULTRASOUND DATA ACQUISITION PARAMETERS

Ultrasound Parameters	Value
Number of elements	128
Pitch	0.30 mm
Operating Frequency	5 MHz
Sampling Frequency	20 MHz
Transmit Focus	35 mm
Speed of sound	1540 m/s
Excitation voltage	50 V
No. Cycles in excitation	2

The ultrasound transducer was positioned at 90° to the microwave heating antenna. The antenna heated the phantom from one side, and the US transducer was positioned on the top surface of the phantom as shown in Fig.1, at a distance of ε=5 mm from phantom edge as shown in Fig.1. The ultrasound transducer was kept at the center covering the middle 15 to 55 mm region of the phantom.

RF data were acquired during the entire 40 min of the experiment. The ultrasound raw RF data were acquired at every ~1 minute interval. The raw RF data after acquisition at sampling frequency of 20 MHz were beamformed using a delay and sum beamformer. Thereafter, Nakagami parameter estimation was performed on the enveloped beamformed RF data to obtain a general Nakagami image, which is explained in Section *D* below.

D. Nakagami parameter Estimation

The Nakagami technique involved dividing the data into an overlapping 1D block each having a size of 80λ, (where λ= 0.32 mm in the US wavelength at 4.8 MHz) The Nakagami parameter was estimated on each block of the data by fitting a Nakagami distribution to it and the value of the shape parameter was computed using a maximum likelihood estimator. The map obtained at this point is known as Nakagami shape parameter map. The problem with this map is the high variability in the estimated parameter values, which is addressed below.

E. Regularization

To reduce the variation in the Nakagami parameter data and make it more generalized, regularization was performed on this data. The regularization was performed using a popular method known as "*Alternating direction method of multipliers"* [12]. The objective function is represented by eq.1.

$$minimize\ \frac{1}{2}\|x-b\|_2^2 + \mu \sum_{i=1}^{n-1} |x_{i+1} - x_i| \qquad (1)$$

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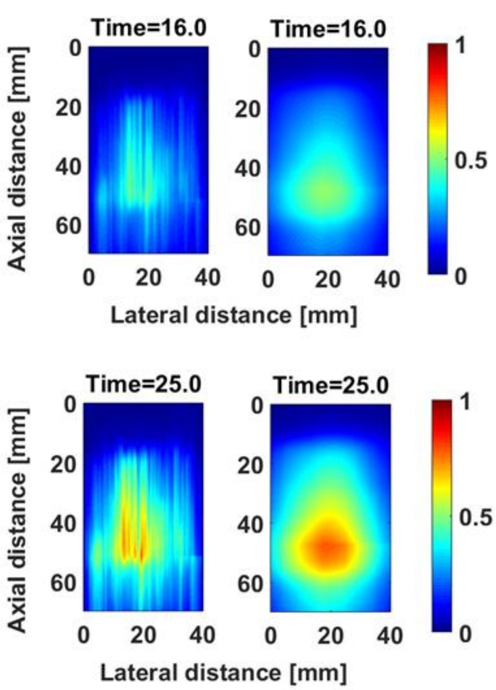
The second term in the equation denotes the total variation of x. In the signal processing literature this problem is also as known as the total variation de-noising, where, b is the estimated log spectral difference data, x is the regularized Nakagami data and μ is the regularization parameter. The value of μ was set as 100. The NCDRN map was finally obtained by taking the difference between two consecutive frames and later accumulating these frames to a particular instant of time.

III. Results

The spatial evolution of normalized cumulative differential Nakagami (NCDN) maps and NCDRN maps at different time points, during the experiment are shown in Fig.2. It can be inferred qualitatively from these maps that the shape and size of the contours evolves with space and time. Also, the regularized images are smoother and are able to capture the spatio- temporal distribution of hotspot more vividly. The contour map of the temperature obtained from the ground truth IR image and the corresponding ultrasound estimated NCDN and NCDRN maps are depicted in Fig. 3 (a), 3(b) and 3(c), respectively. The qualitative comparison shows good correspondence between the temperature contours obtained from IR thermal camera and that from NCDRN map. The time evolution of the NCDRN map during the entire duration of the experiment was captured by computing the mean value of NCDRN map in the ROI as shown in the Fig. 3(d). Quantitative comparison between the map obtained at t=30 min and the ground truth was done by estimating the coordinates of the centroid, the lateral and axial extents of the contour and the area enclosed by the contour that is at 90% of the maximum value. The results are tabulated in Table II. The standard deviation was computed by performing 5 independent experiments.



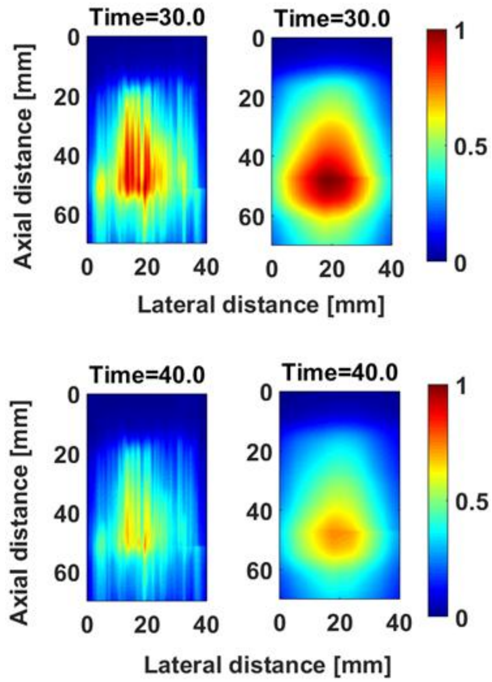


Fig. 2. Images depicting the spatio-temporal evolution of normalized cumulative difference Nakagami (NCDN) map (left column) and normalized cumulative difference regularized Nakagami (NCDRN) maps (right column) at 4 different time points, during the microwave hyperthermia experiment with electric power of 12 W and at a distance of 5 mm from the applicator. The microwave heating was stopped at t=30 min.

Further, the temporal evolution of the NCDRN map at a particular region of interest (ROI) was captured by computing the mean value within the circular ROI of radius 5mm (Fig. 3 (d)), during the entire duration of the experiment. The plot in Fig. 4(a) depicts this evolution of hotspot during the entire 40 minutes of the experiment. Quantitative analysis also involved calculation of the area enclosed by -3 and -6 dB contour threshold, respectively. The plot shown in Fig. 4(b) presents the evolution of it during the duration of the experiment.

TABLE II. Estimated Contour parameters

Parameter	Centroid	Area (cm^2)	Axial extent	Lateral extent
Ground Truth	(19.92,47.06)	2.64	19.18	17.52
NCDRN Estimated	(19.53± 0.34, 48.52 ± 1.44)	1.00 ±0.45	10.39±1.43	12.29 ±1.72

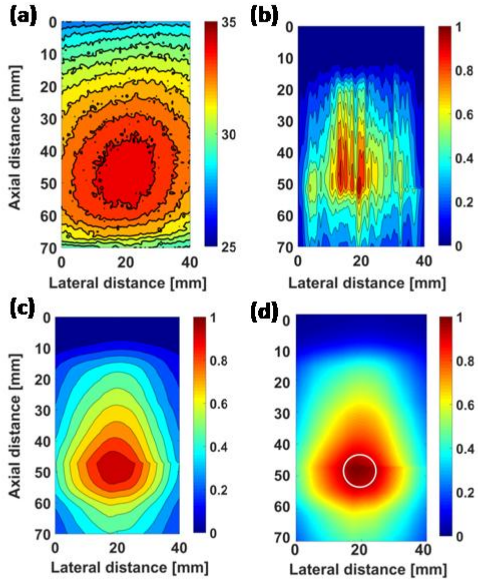


Fig. 3. (a) Contour map of temperature obtained from IR thermal camera; (b) Ultrasound estimated Nakagami parameter contour map; (c) ultrasound estimated regularized Nakagami contour map; (d)Regularized Nakagami map showing the ROI for hotspot (white circle). (Power=12 W,D= 5mm, t=30 min, 434 MHz).

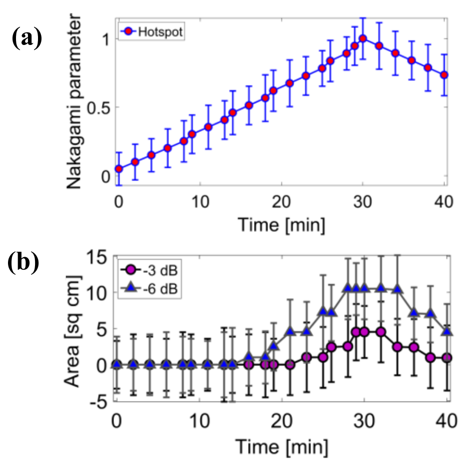


Fig. 4. (a) Plot depicting the evolution of mean value within the ROI of hotspot, shown by white circle in Fig.3(d); (b) Plot showing the area enclosed by -3 and -6 dB contours of NCDRN map for different time instances.

IV. DISCUSSION

The NCDRN map estimated from ultrasound RF data has the potential to estimate the hotspot location and track its spatio-temporal evolution. Also, since ultrasound has an inherent advantage of high frame rate, it can be utilized along with microwave hyperthermia to provide image guidance during microwave hyperthermia treatment. The Nakagami maps have been used to monitor the ablation treatments, but its application in lower temperature regimes typically encountered in microwave hyperthermia has not been explored much. The variability in the local estimates of the Nakagami parameter has been the major drawback. The regularization of the Nakagami parameter estimation technique helps to reduce this variation and provides a way to obtain a more reliable Nakagami parameter estimates. The analysis of the contour maps of temperature from ground truth and NCDRN map demonstrates a good agreement. The difference between the estimated and true centroid location is only 0.39 mm and 1.46 mm in lateral and axial direction, respectively. The error in the area enclosed by contour that is set at 90 % of the maximum value is 62.12 %.This error shows that the regularized Nakagami map underestimated the area compared to ground truth temperature map from IR thermal camera.

V. CONCLUSION

A regularized Nakagami technique was developed and the feasibility of using this to track the spatio-temporal evolution of the hotspot during the microwave hyperthermia has been demonstrated through experiments on *in-vitro* phantom.

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