COST EMF - MED (Action BM1309):
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STSM Report:

Test of Novel Focusing Procedures in an actual Hyperthermic System

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Abstract:

Current hyperthermia (HT) systems are based on multi antenna phased array applicators whose excitations are properly designed during interactive hyperthermia treatment planning (HTP) with real time optimization in order to avoid or reduce the impact of treatment limiting hot spots. The main objective of this STSM is to assess some focusing techniques (Constrained Power Focusing (OCPF) and Optimized Time Reversal (OTR) approach), which have been developed at Università Mediterranea di Reggio Calabria, as two possible strategies to improve the focusing performances of a clinical hyperthermic system designed at Erasmus MC, by optimizing its applicator's excitations. The STMS's positive outcome has set new directions for future optimization of HT treatment planning and the basis for a close and fruitful cooperation between the two research institutions.

A. Purpose of the STSM

The complexity of the anatomy and physiology of the human body set challenges in hyperthermia (HT) therapy which can only be tackled by performing an adaptive treatment policy tailored to the individual patient.

Achieving optimum target temperatures is often hampered by hot spots in healthy tissues, which limits the clinical outcome of the HT treatment. Hence, antenna array applicators are required that are specifically designed to prevent hot spots occurrence. Besides defining the most suitable, application-specific, arrangement and radiating element design, optimum treatments also require the development of the best focusing method. This method should enable to synthesize the complex excitations distribution that feeds the antennas such that a successful HT treatment is achieved.

This STSM was aimed at performing a numerical assessment of the Optimal Constrained Power Focusing (OCPF) [1, 2] and Optimized Time Reversal (OTR) [3] approach, developed at *Lab for ElectroMagnetic Methodologies and Applications* (LEMMA)-Università Mediterranea di Reggio Calabria, as two possible strategies to improve the focusing performance of a clinical hyperthermic system developed at Erasmus MC [4-6], by optimizing its applicator's excitations.

The ultimate goal of this STMS is to establish a fruitful cooperation between the two research institutions for future development of customized optimization solutions for HT treatment planning.

B. Work Description

OTR and OCPF are two focusing strategies developed for improving current focusing methods acting respectively on shaping the E-field and power distribution. OTR is based on the Time Reversal optimization by properly choosing the polarization of the test source [3]. Time Reversal, which relies on the time invariance of

Table 1. SAR based statistics: red/green OCPF row when PSO/OCPF outperforms OCPF/PSO, yellow OCPF row when OCPF outperforms PSO just in terms of tumor coverage.

		TC25 [%]	TC50 [%]	TC75 [%]	THQ
Patient 3024	**PSO**	95	62	10	0,98
	OCPF	93	40	2	0,83
Patient 3014	**PSO**	**99**	85	40	1,68
	OCPF	100	90	45	1,49
Patient 3004	**PSO**	88	72	40	1,77
	OCPF	88	56	12	0,93
Patient 3002	**PSO**	83	69	21	1,2
	OCPF	85	46	11	0,95
Patient 3001	**PSO**	78	34	9	2,11
	OCPF	93	66	30	1,38
Patient 2987	**PSO**	95	70	31	1,39
	OCPF	99	82	39	1,29
Patient 2954	**PSO**	92	58	17	1,42
	OCPF	100	67	17	1,52
Patient 2941	**PSO**	19	5	2	1,08
	OCPF	66	24	6	1,05
Patient 2926	**PSO**	98	68	15	1,61
	OCPF	99	87	33	1,38
Patient 2925	**PSO**	60	28	7	4,95
	OCPF	75	36	11	1,96
Patient 2918	**PSO**	94	56	14	1,54
	OCPF	99	71	29	1,28
Patient 2888	**PSO**	23	8	2	1,38
	OCPF	76	39	12	1,19

the wave equation in lossless media, is not able to keep under control the field intensity in healthy tissues. OTR aims at exploiting the degrees of freedom deriving from the test source polarization in such a way to improve the basic TR in terms of power deposition and, consequently, hot spots raising in healthy tissues.

OCPF relies on the formulation of the focusing problem as a/several Convex Programming (CP) one/s (according to the scalar or vector field's nature), which allows the enforcement of upper bound constraints on the power deposition, guaranteeing to reach the real optimal solution. OCPF and OTR have been demonstrated to be a valid alternative to the existing HT array optimization tools in simplified array configurations. OCPF and OTR performance assessment and test in optimizing the array configuration of a realistic HT applicator, such as HYPERcollar3D [4-6], has highlighted some crucial aspects whose analysis will be beneficial to the actual effectiveness improvement of current HT patient-specific treatments.

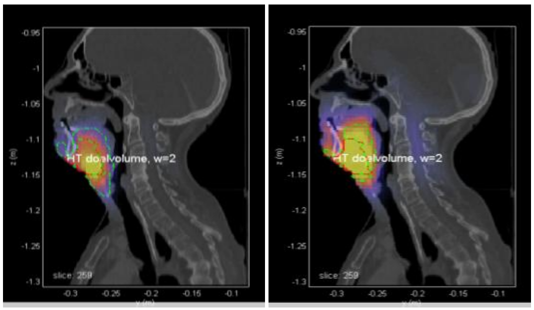
First of all, OTR and OCPF have been customized according to the application requirements. Some programming activities were necessary to integrate the overall code into the existing HT planning tools, VEDO, currently used at Erasmus MC [4, 6].

After merging the codes and proper debugging procedures, OTR and OCPF performances have been assessed numerically, simulating the HT treatment when the array applicator is fed by the corresponding optimized excitations. A comprehensive power deposition analysis has been performed considering 12 patients affected by head & neck tumors of various dimension, shape and collocation. Results are reported in the following.

C. Results

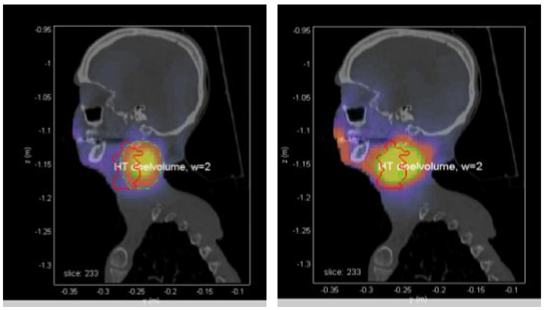
The numerical assessment of the analyzed focusing procedures in a clinical environment has lead to unexpected results which have highlighted new research directions for improving current HTP tools. The analysis aimed at evaluating the focusing capabilities of HYPERcollar3D [4-6] when fed by OTR and OCPF optimized excitations in terms of power deposition into the target area and healthy tissues. In this respect, the metric parameters which have been appraised are Target Coverage 25%-50%-75% (TC25, TC50, TC75) and Target to Hotspot SAR quotient (THQ) [4].

TC25, TC50, TC75 represent the fraction of target volume covered by 25%, 50% and 75% iso-SAR, respectively, i.e. the percentage of target volume (V_{target}) in which the SAR (Specific Absorption Level) level is higher than



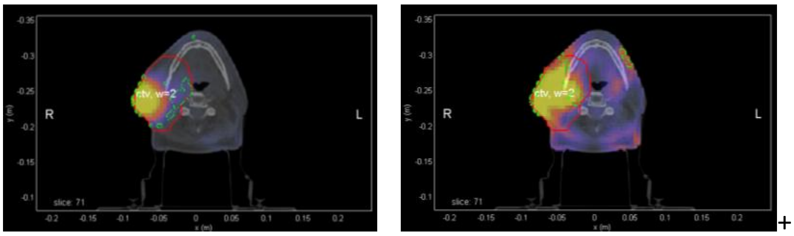
(a) (b)

Fig. 1. Patient 3001. Cf-SAR in the sagittal plane crossing the CTV center: (a) PSO based VEDO and (b) OCPF optimization.



(a) (b)

Fig. 2. Patient 3004. Cf-SAR in the sagittal plane crossing the CTV center: (a) PSO based VEDO and (b) OCPF optimization.



(a) (b)

Fig. 3. Patient 2888. Cf-SAR in a sagittal plane crossing the CTV center: (a) PSO based VEDO and (b) OCPF optimization.

25%, 50% and 75% of the maximum SAR level in the patient. Those parameters were evaluated using spatially averaged SAR over a volume of 1 ml to reduce the effect of possible high-level SAR artifacts (Cf-SAR).

THQ is defined as the ratio between the mean SAR in the target volume and the average SAR in 1% of the volume outside the target with the highest SAR values. This quantifier provides an indication of the prominence of hot-spots relative to the target SAR. As target volume, we have considered the so called Clinical Target Volume (CTV) as defined in Radiotherapy, i.e. the Gross Tumour Volume (GTV) plus a margin for sub-clinical disease spread [7]. Differently from [4-6], we have assumed 20 power channels in such a way to avoid the selection of 12 antennas, whose excitations have to be optimized, because the selection criteria may bias the current results. Please refer to [5] for more details about HYPERCollar3D and PSO based VEDO optimization.

OTR provided poor focusing capabilities compared to the currently used PSO optimization. Those results are mainly due to the intrinsic TR inability to control the field intensity in healthy tissues and stressed the insufficiency of the degrees of freedom related to the test source polarization to cope with it.

Unexpectedly, even OCPF underperforms VEDO optimization when applied in its vector formulation [1]. This is due to the fast depolarization phenomenon that occurs in the treated area, where the penetrated field experiences strong electromagnetic discontinuities related to the human anatomy. The impact of those discontinuities is further increased by the numerical errors. These can be counteracted in the post-processing phase by considering average SAR. This depolarization phenomenon particularly affects OCPF vector formulation because it aims at adjusting the polarization of the field into a target point in the CTV area, in such a way to maximize the power deposition into that point while keeping it under predefined values in healthy tissues [2]. Notably, applying OCPF to the maximization of the power associated to the dominant component of the field, while setting upper bound constraints to the overall power deposition, provides better results. This alternative strategy allows the reduction of the depolarization effects on the optimization procedure providing absolute better focusing capabilities in 33% of patients. In patients affected by irregularly shaped tumours, i.e. the 25%, OCPF underperforms PSO. In the remaining percentage of patient PSO, i.e. 44%, OCPF outperforms VEDO optimization in terms of target area coverage paying a fee in terms of THQ, that should be acceptable. An example of the latter case is shown in Fig. 1.

We can conclude that the shape and dimension of the tumour seem to influence OCPF performance because of the upper bound constraints that have to be set into the healthy tissues. Of course, those constraints have to be properly established to avoid restricting the search space to the point that on the null solution is included. Of course, the working frequency plays an important role in establishing those settings. These are currently fixed according to the conductivity profile in healthy tissues to impose stricter values where the conductivity is higher and, hence, the SAR is expected to be higher.

It is important to stress that even in those cases when OCPF underperforms VEDO optimization according to the metrics presented in Table 1, e.g. patient 3004, it shows some important capabilities such that of being able to control the focusing process into the target point. In fact, as shown in Fig.2, even if OCPF provides an overall worse coverage capability of the target area it is able to focus the power deposition into the CTV's center. This is an important aspect that may have a huge impact in the quality of the provided HT treatment.

It is also worth to note that OCPF is a valuable alternative to the basic VEDO optimization, making treatments feasible for patients that would be excluded when applying PSO (see Patient 2888 in Table 1 and Fig. 3).

In conclusion, considering the small amount of time and the number of unforeseeable crucial aspects that emerged during these research activities, the preliminary results presented in this report are remarkable. The actual benefit must be validated using temperature simulations, but current results already set new directions for future optimization of HT treatment planning.

D. Future collaboration with host institution

The study conducted during this STMS has enlightened some critical aspects of the focusing process required during an head & neck HT treatment, which have not been taken into account during the development of the assessed focusing approaches. Thanks to the interaction between the members of the involved institutions new ideas and possible solutions also have been produced and will be developed in the following months.

First of all, some arrangements have already been set up to finalize the thermal validation of the presented results by the researcher who was recipient of this STSM. Hereto, Erasmus MC organized access to the thermal simulation tool for analysis at Università Mediterranea di Reggio Calabria. In addition, Zurich MedTech (ZMT) AG is in the process of providing a one year academic free license of Sim4Life for Science platform to perform the thermal analysis [8].

Alternative optimization procedures, such as multi-target approaches or new average power based cost functions, will be developed in the framework of an Italian research project, entitled *Field And Temperature Shaping and Monitoring for Microwave hYperthermia* (FAT SAMMY), commonly submitted to the Italian Research Ministry (MIUR) and, currently, under evaluation. Other possible funding requests are under discussion to further boost and support the novel collaboration.

E. Expected Publications

Preliminary results of this work have been submitted as a conference contribution to ICHO 2016 and to BioEM meeting, which will be held in New Orleans in April 2016 and Ghent (Belgium) in June 2016, respectively. The comprehensive study is expected to be submitted to a peer review journal in the next months.

F. Other Comments

We kindly acknowledge ZMT Zurich MedTech AG (www.zurichmedtech.com) [8], for providing a one year academic free license of Sim4Life to Università Mediterranea, allowing the prosecution of this work.

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[8] Sim4Life by Zurich MedTech AG, www.zurichmedtech.com

Confirmation by the host institution of the successful execution of the STSM:

We confirm that Domenica A. M. Iero has performed the research work as described above.

Prof. Gerard Van Rhoon Dr. Domenica A. M. Iero