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Selecting the Optimal Subset of Antennas in Hyperthermia Treatment Planning

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Abstract—Hyperthermia treatment planning is a deeply patient-specific task which includes the optimal determination of the excitations of an array applicator. To enhance flexibility, various solutions exploiting different frequencies, antenna element, number, and applicator geometries have been proposed in the literature. Amongst them, increasing the frequency and the number of radiating elements have been effective for achieving more conformal heating. However, as each radiating element requires a power amplifier to control it, increasing the number of antennas considerably impacts the overall cost and complexity of the system. Accordingly, a procedure capable of selecting an optimal patient-specific subset of antennas from an oversized phased array applicator (with more antenna elements than available amplifiers) could help improve cost-effectiveness. In this study, we present an original approach, which allows improving performance by adaptively selecting the optimal subset of antennas to be activated for a given (redundant) applicator and a given patient. The proposed approach takes inspiration from the compressive sensing theory by embedding the sparsity promotion paradigm into a treatment planning procedure, which casts power deposition as a constrained convex optimization. Performances were demonstrated for the case of head and neck hyperthermia and benchmarked against the antenna selection procedure presently used in clinical practice.

Index Terms—Compressive sensing, hyperthermia treatment planning, Convex Programming, constrained power optimization.

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I. INTRODUCTION

HYPERTHERMIA is a selective increase of the tumor temperature to a supra-physiologic temperature (40–44 °C) for 60–90 min. Clinical trials have demonstrated the therapeutic benefit of this treatment in combination with radio- and chemo-therapy [1], [2]. According to the thermal dose-effect relations found in literature [2], [3], temperature increase would further enhance the clinical effectiveness. Focused deep heating is achieved using fully active phased antenna array applicators operating in the MHz range. Further progress and widespread clinical adoption of hyperthermia are dependent upon an accurate pre-treatment optimization and real-time adaptations of the administered heating [4]. This task includes the design of both the applicator [5]–[8], as well as of the complex excitations (phases and amplitudes) feeding its elements.

Amongst hyperthermia researchers, there is still no consensus concerning the choice to be pursued on whether the specific absorption rate (SAR) or temperature distribution should be optimized. In the literature, treatment quality surrogates based on both the predicted SAR and temperature distribution have been proposed and optimized [9]–[14]. On one side, temperature-based optimizers should allow in principle to get a better control of the actual variable of interest (i.e., the temperature distribution). However, such an approach deeply depends on thermal tissue properties, whose knowledge is affected by a very large uncertainty [15]. Additionally, global optimizers (prone to sub-optimal solution [16]) are presently required, with considerable requirements in terms of computational burden. Hence, also in view of the argument in [17], optimizing the SAR distribution has been considered. While contrasting results can be found in the literature [9], optimizing the SAR pattern is, anyway, faster than temperature optimization since such a task does not involve the solution of the bio-heat transfer equation as well. Furthermore, SAR can also be experimentally validated within a quality assurance procedure and computationally controlled [16]. Last but not least, SAR optimization can be pursued by convex optimizers [16]. Hereto, local minima absence allows operator-independency, thus being viable for real-time operations.

Parallel to an optimal treatment planning strategy (either SAR- or temperature-based) for a given system (and given patient), a key ingredient of microwave hyperthermia is obviously the design of the phased antenna array applicator. This task involves different aspects. By increasing the frequency, for instance, a more target conformal heating pattern can be achieved,

although a price is paid in terms of a reduction of the penetration depth (thus lower SAR levels). For a fixed frequency, the heating pattern can be optimized by both increasing the number of transmitting elements (coherently with [18]) and/or optimizing the array layout [7].

The need of treating tumors positioned in different anatomical regions triggered researchers to propose different applicators with various geometries, (larger) antenna element number and working frequency, e.g., the RHOCs system (18 antennas), the BSD-2000 Sigma-Eye (12 antennas), the AMCs systems (four/eight antennas) [13], the head and neck applicators from Trefná *et al.* (10/16 antennas) [19], [20], the hybrid MRI system (8/16 antennas) from the group of Winter *et al.* [21], [22] and the HYPERcollar3D (20 antennas) [23]. As a general concern, given the necessary patient-specific nature of the problem, increasing the number of radiating elements may represent a straightforward strategy to improve both target conformal heating pattern as well as steering capabilities, as it would enable a larger number of degrees of freedom contributing to the optimization. However, each radiating element requires a power amplifier which, because of the required specifics, has a non-negligible impact on the overall system cost [23]. As a result, taking into account that only a limited number of amplifiers are usually available, and that each treatment is strongly case-specific, the development of an antenna selection procedure is advisable.

In this work, we deal with the problem of minimizing/reducing the active elements number of a given applicator needed to maximize, for a given patient, the SAR within the target volume and, at the same time, avoid undesired heating in healthy tissues. To this end, the sparsity of the solution, i.e., the complex excitation coefficients, is promoted by profitably borrowing concepts from the compressive sensing (CS) theory [24], [24]–[26].

In the following, we present and test the feasibility of a novel optimization tool that is able to optimally select a desired number of active antennas from a given applicator able to maximize the SAR deposition in a target volume while avoiding hot-spot occurrence. The proposed approach determines the optimal active elements configuration (and the corresponding excitations) exploiting all possible constructive and/or destructive interference of the fields generated by each element of a given applicator. The development of the proposed approach takes advantage both from Focusing via Constrained power Optimization (FOCO) [16] and from the CS theory [24], [27]. Interestingly, the proposed approach, named sparsity promoted FOCO (SP-FOCO), allows determination of the globally optimal solution using local search algorithms as we are able to formulate the overall problem as a Convex Programming one. The performances of SP-FOCO have been then tested on fifteen 3D patient models planned for the HYPERcollar3D [23] and the results benchmarked against the present clinical antenna selection approach.

It is worth noting that, while the methodology is herein presented and exploited with respect to the problem of selecting a subset of the radiating elements for a fixed system, it can be also useful in the design of applicators using a minimally redundant number of elements, by refining an oversized implementation made by a (very) dense array. However, also in view of the

difficulties arising in properly handling mutual coupling in such a design procedure, this possible development is not considered in the present contribution.

II. MATERIALS AND METHODS

A. The Proposed Approach: Sparsity Promoted FOCO

Indicating with σ the conductivity [S/m], ρ the mass density [kg/m³] and with $|\mathbf{E}(\underline{r})|^2$ the squared amplitude of the total electric field generated by properly weighted N monochromatic sources surrounding a 3D region of interest Ω , the SAR is given by

$$SAR(\underline{r}) = \frac{\sigma(\underline{r})}{2\rho(\underline{r})} |\mathbf{E}(\underline{r})|^2 \quad (1)$$

where $\underline{r} \in \Omega$ is a generic point of Ω . The overall total electric field, i.e., $\mathbf{E} = E_x \mathbf{i}_x + E_y \mathbf{i}_y + E_z \mathbf{i}_z$, in a generic $\underline{r}$ can be expressed as

$$\mathbf{E}(\underline{r}) = \sum_{n=1}^N I_n \Phi_n(\underline{r}) \quad (2)$$

where $\Phi_n = \Phi_{x,n} \mathbf{i}_x + \Phi_{y,n} \mathbf{i}_y + \Phi_{z,n} \mathbf{i}_z$ is the total electric field induced by the unitary excited n -th antenna in Ω when all the other antennas are off and $I_n (n = 1, 2, \dots, N)$ represent the complex excitation coefficients feeding the elements of the applicator.

The proposed approach is based on our recently clinically tested FOCO [16]. With respect to this latter, one has to add that just a certain number of antennas (L) amongst the whole array set (N_{wa}) can be excited with amplitudes different from zero. Thus, the problem can be formulated:

Find $I_n (n = 1, \dots, N)$ such that

$$\max \{ |\mathbf{E}(\underline{r}_t)|^2 \} \quad (3a)$$

subject to

$$|\mathbf{E}(\underline{r})|^2 \leq \mathcal{MF}(\underline{r}) \quad \underline{r} \in \Omega \setminus \Pi(\underline{r}_t) \quad (3b)$$

$$\|I_n\|_{l_0} \leq L \quad (3c)$$

where $\|\cdot\|_{l_0}$ is the pseudo l_0 norm (counting the number of elements different from zero in the sequence). Here, $\mathcal{MF}(\underline{r})$ is a “mask” function that allows enforcing patient-specific hot-spot avoiding constraints. This latter, according to [16], can be set as $\mathcal{MF}(\underline{r}) = A/(\sigma_N(\underline{r}) + A)$, where $\sigma_N(\underline{r})$ represents normalized conductivity distribution into the patient and A is a scalar value set according to [16]. As a consequence, the maximum allowed electrical field value in normal tissue is bounded according to a precise SAR based criterion. The target area, i.e., Π_{FOCO} , is defined as a non-isotropic volume expansion of the so-called hyperthermia target volume (HTV) which, following Radiotherapy, generally corresponds to the clinical target volume plus some margin [28]. For further details, see [16].

Unfortunately, the optimization problem (3) is a very hard one (belonging to the NP-class hard class [29]). As discussed in [16], a first simplification can be gained when one of the field components ($E_i(\underline{r})$) can be considered to be dominant above the other ones. Then, let us also note that the phase reference in the target

point is a free parameter. In fact, without any lack of generality, we can assume that the field in the target point is purely real. Hence, the optimization function (3a) can be profitably modified into

$$\max \{\Re\{E_i(r_t)\}\}. \quad (4)$$

Finally, inspiration from the CS theory can be taken [24]–[26]. This latter shows that, in optimization (or reconstruction) problems the l_0 pseudo-norm can be often and conveniently relaxed into the l_1 -norm. In fact, provided a number of hypotheses are fulfilled [24], [25], such a relaxation is “free of charge”, in the sense that the global optimum keeps unchanged with respect to the original problem. Hence, by exploiting the above relaxation of the cost function and of constraints (3c), formulation (3) can be conveniently written as

Find I_n ($n = 1, \dots, N$) such that

$$\max \{\Re\{E_i(r_t)\}\} \quad (5a)$$

subject to

$$\Im\{E_i(r_t)\} = 0 \quad (5b)$$

$$|\mathbf{E}(r)|^2 \leq \mathcal{MF}(r) \quad r \in \Omega \setminus \Pi(r_t) \quad (5c)$$

$$\|I_n\|_{l_1} \leq \epsilon \quad (5d)$$

where $\Re\{\cdot\}$, $\Im\{\cdot\}$ indicate real and the imaginary part, respectively, and ϵ a parameter to be tuned.

Constraints (5b)–(5d) define a convex set in the space of the unknowns [30]. The cost function (5a) is a linear function of the unknowns. Hence, formulation (5) is now conveniently cast as a Convex Programming problem. As such, the globally optimal solution can be efficiently determined via local optimization procedures.

The proper tuning of the sparsity parameter ϵ has a pivotal role in the optimization process [26], [31]–[34]. In our specific application, we aim at selecting N_A antennas out of the N_{wa} elements of the whole array. As such, large values of ϵ will determine a large number of complex excitation coefficients different from zero, so that the required number of antennas may result larger than the number of available amplifiers. In a dual fashion, small values of ϵ would imply not taking advantage from all the available amplifiers. A possible choice is to set ϵ equal to a fraction of ϵ_{wa} defined as the average $\|I_n^{wa}\|_{l_1}$, where I_n^{wa} are the complex excitations coefficients obtained when optimizing the whole applicator [26]. An intuitive choice could be to set ϵ equal to $N_A/N_{wa}\epsilon_{wa}$.

A common practical drawback of sparsity-promotion-based approaches¹ is that they aim at setting to zero a certain amount of complex excitation coefficients, but the actual number is not ensured. Therefore, in order to tackle such a limitation, a two step procedure has been devised and schematically depicted in Fig. 1. Indicating with N_A the number of available amplifiers, the procedure is given in the following:

- 1) The complex excitations coefficients I_n are determined through the proposed SP-FOCO.

Fig. 1. Schematic view of the proposed SP-FOCO. M indicates the number of active elements identified by SP-FOCO and N_A the desired number of active elements, i.e., the number of available amplifiers.

- 2) Evaluate M as the number of excitation coefficients different from zero.
- 3) If $M \leq N_A$, M antennas can be exploited in the treatment.
- 4) If $M > N_A$, a thresholding procedure is applied [26].

In case the number of active antennas is larger than the available amplifiers, i.e., $M > N_A$, our thresholding procedure aims at setting to 0 the $M - N_A$ antennas exhibiting lower weights in terms of $|I_n|$, as schematically depicted in Fig. 1.

Obviously, such a possible thresholding implies some deterioration of performances; which has to be evaluated (see also Section IV).

B. Evaluation Setup

The evaluation dataset consists of fifteen 3D head & neck patient models that were planned for treatment with the HYPERcollar3D [23].

The HYPERcollar3D consists of a ring-shaped phased array of twenty patch antennas arranged over three rings and operating at 434MHz. The applicator design aims at constructive interference, so generally the field component along the main axis of the body, z -component, could be considered as dominant. A water bolus fills the space between the applicator and the patient to enhance electromagnetic coupling and to avoid undesired heating that may arise at the patient’s skin [23].

Patient-specific models were created following the guidelines in [12]. The procedure starts by delineating the various tissues based on computerized tomography scans using a custom atlas-based auto segmentation routine followed by a manual adjustment in software tool iSeg (v.3.8 Zurich Medtech, Zurich, Switzerland) [35]. Segmented tissues were associated to electromagnetic tissues parameters accordingly to [12], [35]. Then, the 3D patient-specific models were imported into Sim4Life (v. 3.4 Zurich MedTech AG, Zurich, Switzerland) and simulated together with the applicator model. The fields $\Phi_n(r)$ were computed for a 1-V sinusoidal signal excitation at the operating frequency for each antenna. To this end, the Visualization Tool for Electromagnetic Dosimetry and Optimisation (VEDO) was used [12].

¹Regardless of the procedure adopted to properly set the ϵ .

In order to quantitatively evaluate the proposed approach, performances have been compared with the clinically adopted antenna selection procedure exploiting FOCO, as from [16], for planning optimization. At the Erasmus MC, such a selection procedure has been devised for the above described HYPER-collar3D applicator [23]. Since twelve amplifiers are available, twelve out of the whole available array elements are selected individually for each patient. The clinical antenna selection approach identifies antenna-wise the twelve Dominant SAR Inducing Antennas (DSIA) within the HTV. This procedure, while being very intuitive, may suffer from the drawback of not exploiting interferences of the electromagnetic fields generated by different antenna subsets. Hence, it also neglects that destructive interference of fields generated from two antennas far from the HTV could counteract (or even avoid) hot-spot occurrence. In the following, evaluation metrics obtained with SP-FOCO were comparatively assessed to FOCO in conjunction with the clinical antenna selection procedure. This has been indicated adding the subscript DSIA, i.e., $\text{FOCO}_{\text{DSIA}}$.

Different ϵ values have been tested. Accordingly to Section II-B, we considered $\epsilon_1 = 12/20\epsilon_{wa}$, $\epsilon_2 = 11/20\epsilon_{wa}$ and $\epsilon_3 = 10/20\epsilon_{wa}$. Here, ϵ_{wa} was evaluated as the $\|I_n^{wa}\|_{l_1}$ averaged on 15 patients where the I_n^{wa} have been obtained optimizing through FOCO when considering 20 antennas.

C. Comparison and Evaluation Metrics

The SAR quality indicators adopted in our study allow a full, while still synthetic understanding of the induced SAR distribution into the patient. The considered quality indicators are the target coverage and the THQ. The target coverage has been evaluated at 25%/50%/75% (TC25/TC50/TC75), and it is defined as the volume percentage of the HTV covered by 25%/50%/75% iso-SAR value when the SAR distribution is normalized to the maximum in the whole patient model. The THQ is defined as the ratio of the average SAR in the HTV and the average SAR in 1% volume of healthy tissue volume where the highest SAR occurs [12]. These standard SAR-based quality metrics, implemented in the clinical tool VEDO, are used for clinical decision making and patient inclusion as they have been correlated to temperature-based quality metrics [36], [37], which have been previously shown predictive for clinical outcome [37]–[41]. In the following, the difference (indicated with Δ) of the considered SAR quality indicators achieved by means of SP-FOCO and $\text{FOCO}_{\text{DSIA}}$ will be analyzed.

Finally, in order to quantitatively assess the impact of the thresholding procedure (see step 4 of the procedure at the end of Section II-A), the so-called thresholding error has been introduced and evaluated. Such a metric indicates the percentage of the truncated energy of the complex excitations (in the $\|\cdot\|_{l_2}$ sense).

III. RESULTS

Fig. 2 depicts the results obtained by means of both $\text{FOCO}_{\text{DSIA}}$ and SP-FOCO when adopting ϵ_1 , ϵ_2 and ϵ_3 . Each graph reports the comparison of one SAR-based quality metric. In each sub-graph, each star represents one patient. Hence, in

Fig. 2. Comparison of SAR-based quality parameter achieved with SP-FOCO and $\text{FOCO}_{\text{DSIA}}$ on TC50 (first column) and THQ (second column) concerning ϵ_1 (first row), ϵ_2 (second row), and ϵ_3 (third row). Cases where $M = 12$, $M = 11$ or $M = 10$ are marked with additional light blue, pink and green circles, respectively.

all cases in which stars appear in the upper (white) triangle SP-FOCO is outperforming $\text{FOCO}_{\text{DSIA}}$. On average, a difference has been observed for ΔTHQ , $\approx +4\%$, and for TC50 which, amongst all, was shown to be the most temperature predictive [36]. Specifically, improvements on ΔTC50 equal to $+6\%$, $+5\%$ and $+4\%$ were found when exploiting respectively ϵ_1 , ϵ_2 and ϵ_3 . A negligible improvement of $\approx +1\%$ was, instead, observed in terms of ΔTC25 and ΔTC75 .

As expected, results show that by lowering the sparsity parameter the number of active elements was reduced. When exploiting ϵ_1 , the procedure was able to identify two cases in which the number of active elements was exactly equal to the available amplifiers, i.e., $M = 12$; see Fig. 2. Surprisingly, when exploiting ϵ_2 and ϵ_1 , the number of active elements in those cases is $M = 11$ and $M = 10$ which is lower than the number of available amplifiers (see Fig. 2). In the other cases where a thresholding procedure was applied, the truncation error was always found to be below 1%.

Fig. 3. Normalized SAR distribution related to case A and B on a axial view obtained by means of $\text{FOCO}_{\text{DSIA}}$ and SP-FOCO.

IV. DISCUSSION

In this study, we have demonstrated the usefulness of SP-FOCO as an innovative tool for hyperthermia treatment planning. The assessment has been carried out in an actual clinical scenario and the outcomes compared to the clinically used antenna selection procedure, i.e., chosen as the dominant SAR inducing antennas [23]. Results showed that on average the proposed approach is, able to slightly outperform the adopted benchmark. Interestingly, significant improvements are anyway achieved in a number of cases. We investigated various sparsity promoting parameter values, ϵ , and this helped setting the most suitable value of such parameter for the case at hand.

The feasibility of exploiting the CS framework in HTP has been herein demonstrated and promising results shown. However, there are few cases in which performances are not improved. This can probably be the price of considering the l_1 -norm rather than the (pseudo-) l_0 -norm [24], [25], [42].

Interestingly, our results showed there is the tendency of SP-FOCO in outperforming $\text{FOCO}_{\text{DSIA}}$ for the deep seated tumors. While a dedicated complete analysis is still lacking, the interest of the procedure is also witnessed from the fact that the subset antenna selected by the proposed SP-FOCO are never equal to the one from the clinically adopted process, i.e., the DSIA ones. In this respect, it is interesting to have a closer look to two cases wherein the HTV is close to the skin surface (case A) and deep-seated HTV (case B). The complex excitations coefficients ($|I_n|$) obtained through $\text{FOCO}_{\text{DSIA}}$ and SP-FOCO exploiting

Fig. 4. Normalized excitation coefficients evaluated through SP-FOCO (first row) and $\text{FOCO}_{\text{DSIA}}$ (second row) for patient A and B, first and second column, respectively.

ϵ_1 and the induced SAR distributions are reported, respectively, in Figs. 3 and 4. Concerning case A, the selected antenna subset inducing the higher SAR in the HTV are dictated by physical and meaningful choices. As such, results of the two optimization approaches are approximately equal (only ΔTHQ was found $\approx +4\%$). In case B, the improvements yielded by SP-FOCO are more evident ($\Delta T50 \approx +14\%$ and $\Delta THQ \approx +4\%$), as well as the selected antenna subset very different from the clinical procedure.

Note we did not assess performance of SP-FOCO as compared to the clinical optimization routine [12]. In fact, in this work one component of the field was assumed to be dominant amongst the others.² However, the clinical optimization routine optimizes the SAR distribution taking into account the whole vector nature of the electric field. Hence, since field depolarization could be exploited for a better solution, we preferred to avoid such a biased comparison. The extension to the case of vector field is however doable following the guidelines in [43].

V. CONCLUSION

In this work, we proved the usefulness of exploiting concepts borrowed from the CS theory in hyperthermia treatment planning for the selection of the optimal antennas subset of a given applicator. The proposed SP-FOCO, based on our clinically tested FOCO, was shown to be suitable for such an aim. The performance of our antenna selection procedure were proven with reference to the HYPERcollar3D for head and neck hyperthermia, and benchmarked against the clinically applied selection procedure. Results show that, on average, SP-FOCO performs comparable to the benchmark ($\Delta TC50 \approx 5\%$), but there is a tendency in outperforming the benchmark for the deeper seated tumors. Interestingly, the selected antenna subsets are very different from the ones selected by the current clinical procedure.

²In [16], we showed that within the HYPERcollar3D, the field component along the main axis of the patient is the dominant one by approximately a ratio of 3 ± 0.8 .

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