RBF-metamodel driven multiobjective optimization and its application in focused ultrasonic therapy planning

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***Abstract*—We consider bi-objective optimization problem from noninvasive tumor therapy planning. The therapy uses magnetic resonance tomography for the location of the target region and focused ultrasound for the destruction of tumor cells. Experimentally validated physical models are used to construct numerical simulation including nonlinear wave propagation, absorption in soft tissue, heat transfer and a hierarchical structure of the biological materials. The resulting cumulative thermal dose inside the target region should be maximized, providing a maximal level of tumor destruction, while the thermal dose outside the target region should be minimized, to decrease the influence to healthy organs. Metamodeling with radial basis functions is used for continuous representation of optimization objectives. The problem possesses nonconvex Pareto front. Detection of nonconvex Pareto fronts is especially difficult, this is a point where many simple algorithms fail. In this paper we consider different approaches to this problem: sequential linear programming (SLP), sequential quadratic programming (SQP) and generic 1- or 2-phase nonlinear programming (NLP). We show the ability of the algorithms to process such case and compare the efficiency of different approaches.**

Keywords-complex computing in application domains; medical computation and graphics; advanced computing in simulation systems; advanced computing for statistics and optimization.

I. INTRODUCTION

Focused ultrasonic therapy is a noninvasive therapy using magnetic resonance tomography for identification of tumor volume and focused ultrasound for the destruction of tumor cells. Numerical simulation becomes an important step for the therapy planning. Efficient methods for the focused ultrasonic simulation have been presented in paper [1]. It uses a combination of Rayleigh-Sommerfeld integral for near field and angular spectrum method for far field computations, which allows determining the pressure field in heterogeneous tissue. The bioheat transfer equation is used to determine the temperature increase in therapy region. Thermal dose is defined according to cumulative equivalent minutes metric (CEM, [2]) or Arrhenius model [3] as a functional of temperature-time dependence in every spatial point in therapy region. These methods have been accelerated by GPU based parallelization and put in the basis of software FUSimlib (www.simfus.de), developed by our colleagues at Fraunhofer Institute for Medical Image Computing.

3D visualization is used for interpretation of simulation results, in particular, for detailed inspection of MRT images (magnetic resonance tomography), corresponding material model and spatial distribution of the resulting thermal dose, see Fig. 1. Stereoscopic 3D visualization in virtual environments based on modern 3D-capable beamers with DLP-Link technology (Digital Light Processing), described in more details in [4] is especially suitable for this purpose. Such commonly available beamers do not require special projection screens and can turn every regular office to a virtual laboratory providing full immersion into the model space. We use 3D visualization software Avango (www.avango.org), an object-oriented programming framework for building applications of virtual environments. Our interactive application overlays three voxel models: original MRT sequence, material segmentation and resulting thermal dose. The user can mix the voxel models together, interactively changing their levels of transparency, set breathing phase, cut the model with a clipping plane, etc.

For continuous representation of optimization objectives from a discrete set of simulation results we use metamodeling with radial basis functions (RBF). It represents the interpolated function f(x) as a linear combination of special functions Φ() depending only on the distance to the sample points x_k:

$$f(x) = \sum_{k=1..Nexp} c_k \, \Phi(|x-x_k|) \qquad (1)$$

The coefficients c_k in (1) can be found from known function values in sample points $f(x_k)$ by solving a moderately sized linear system with a matrix $\Phi_{kn} = \Phi(|x_k-x_n|)$. A suitable choice for the RBF is the multi-quadric function $\Phi(r)=(b^2+r^2)^{1/2}$, which provides nondegeneracy of interpolation matrix for all finite datasets of distinct points and all dimensions [5]. RBF interpolation can be extended by adding polynomial terms, allowing reconstructing exactly polynomial (including linear) dependencies and generally improving precision of interpolation. Adaptive sampling and hierarchy of metamodels with appropriate transition rules are used for further precision improvement. RBF metamodel is directly applicable for interpolation of high dimensional bulky data, e.g. complete simulation results can be interpolated at a rate linear in the size of data, and even faster

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in combination with PCA-based dimensional reduction techniques. The precision can be controlled via cross-validation procedure. So enhanced RBF metamodel is a part of our software tool for design parameter optimization DesParO [6-8].

The objective of therapy planning is a maximization of thermal dose inside the target zone (TDin) and minimization of thermal dose outside (TDout). As usual in multi-objective optimization, the optimum is not an isolated point but a hypersurface (Pareto front, [9]) composed of points satisfying a tradeoff property, i.e. none of the criteria can be improved without simultaneous degradation of at least one other criterion. Thus, for a two-objective problem, the Pareto front is a curve on the plot (TDin, TDout) bounding the region of possible solutions. Efficient methods have been previously developed for determining the Pareto front.

The simplest way is to convert multi-objective optimization to single objective one, by linearly combining all objectives into a single target function

$$t(x)= \sum w_i f_i(x) \qquad (2)$$

with user-defined constant weights w_i. Maximization of the target function (2) gives one point on Pareto front, while varying the weights allows to cover the whole Pareto front. In this way only convex Pareto fronts can be detected, because nonconvex Pareto fronts produce not maxima but saddle points of the target function.

There are methods applicable also for nonconvex Pareto fronts. Nondominated set algorithm (NDSA) finds a discrete analogue of Pareto front in a finite set of points. For two points f and g in optimization criteria space the first one is said to be dominated by the second one if $f_i \le g_i$ holds for all i=1..Ncrit. A point f belongs to nondominated set if there does not exist another point g dominating f. There is a recursive procedure [10] finding all nondominated points in a given finite set. The drawback of the algorithm is an extremely large number of samples necessary to populate multidimensional regions for good approximation of Pareto front.

Normal boundary intersection method (NBI) [11] provides a good heuristics for sampling of Pareto front. The idea is to find individual minima of objectives, to construct their convex hull, to sample it e.g. with Delaunay tessellation, to build normals in tesselation points and finally to intersect them with the boundary of par → crit mapping. The approach has problems e.g. at Ncrit>2, when non-Pareto points or not all Pareto points are covered, or if the number of minima >Ncrit, when several local Pareto fronts can be mixed together.

Meanwhile, practical applications just require an elementary algorithm performing a local improvement of current design towards the optimum. Being iterated such algorithm proceeds towards Pareto front. For definiteness, an improvement direction in the space of objectives can be fixed, e.g. every step all objectives are improved by a given increment. The algorithm stops when the further improvement in the given direction is not possible. Normally it happens when the solver reaches the Pareto front. Convex or nonconvex Pareto fronts can encounter and the algorithm should work equally efficient for both. The improvement can also stop on a non-Pareto boundary point. In this case it is allowed to return the other point on Pareto front, which does not necessarily belong to the original improvement direction.

In further sections we consider different approaches for this algorithm: sequential linear programming (SLP), sequential quadratic programming (SQP) and generic 1- or 2-phase nonlinear programming (NLP). We also consider a question of scalarization, i.e. a possibility to reformulate the multiobjective optimization problem as constrained optimization with a single objective, which allows to employ available NLP solvers for its solution.

II. USING SEQUENTIAL LINEAR PROGRAMMING

Linearizing the mapping y=f(x) using Jacoby matrix $J_{ij}=\partial y_i/\partial x_j$, let's consider a polyhedron of possible variations

$$\Pi_\varepsilon: \Delta y=J\Delta x\ ,\ \Delta y \ge \varepsilon > 0\ ,\ -\delta \le \Delta x \le \delta, \qquad (3)$$
$$x_{min} \le x+\Delta x \le x_{max}\ ,\ y_{min} \le y+\Delta y \le y_{max}$$

Here we require that all criteria Δy are improved, parameter variations Δx are bounded in a trust region $[-\delta,\delta]$ for linear approximation, while parameters and criteria satisfy bounding box or other polyhedral restriction in xy-space. By requiring in (3) that a maximally possible improvement of criteria in Π_ε is achieved, we formulate a linear program which can be solved e.g. by simplex method [12] and repeated sequentially:

Algorithm SLP:

Solve LP: max ε, s.t. $(\Delta x,\Delta y)\in\Pi_\varepsilon$

Repeat steps $x+\Delta x \rightarrow x$ until convergence.

The algorithm terminates at Pareto front, where no further improvements are possible.

Property: in general position LP-optimum is achieved in corners of polyhedron Π_ε.

E.g. $\Delta y=\varepsilon$ correspond to linear trajectories in y-space, $|\Delta x|=\delta$ correspond to linear trajectories in x-space. Therefore, the method tends to generate linear trajectories in certain projections.

SLP above is formulated for the case dim(x)=dim(y). At dim(x)<dim(y) multiobjective problem is ill defined, i.e. full dimensional regions in parameter space become Pareto equivalent. At dim(x)>dim(y) there are unstable directions from Ker(J): $J\Delta x=0$, i.e. there are Δx not influencing Δy. These directions can be suppressed by additional condition $J_\perp \Delta x=0$, where $J_\perp$ is orthogonal complement to J, constructed e.g. with Gram-Schmidt algorithm.

Example: let's consider a fold transform: $|y|=2|x|/(1+|x|^2)$ shown on Fig. 3 for 2D case. An upper right arc corresponds to a global Pareto front (PF) max y_1,y_2. There is also a

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degenerate local PF at $y_{1,2}$=-0, corresponding to an image of $x_{1,2}=-\infty$.

SLP algorithm generates trajectories shown by red lines on Fig. 3, in x-space in the left column and in y-space in the right column. The algorithm reconstructs correctly both global and local PF, shown by blue points on the images. The bottom closeups demonstrate piecewise linear trajectories described above. Particularly, there is a dashed linear trajectory in y-space tending to non-Pareto part of the boundary (nPF), which at a certain moment switches from $\Delta y=\varepsilon$ corner to $|\Delta x|=\delta$ corner, becomes curved and finally stops at PF.

III. USING SEQUENTIAL QUADRATIC PROGRAMMING

Polyhedron Π_0 is defined as above (with $\varepsilon=0$). Let v be a fixed search direction in y-space, ε is a constant. The following quadratic program [15] tries to perform $\Delta y=\varepsilon v$ steps if possible in Π_0:

Algorithm SQP:

Solve QP: min $||\Delta y-\varepsilon v||^2$, s.t. $(\Delta x,\Delta y)\in\Pi_0$
Repeat steps $x+\Delta x \rightarrow x$ until convergence.

Property: in general position QP-optimum can be achieved inside Π_0, in corners of Π_0 or on edges/faces of Π_0.

In the first case $\Delta y=\varepsilon v$ linear trajectories will be generated in y-space, in the second case $|\Delta x|=\delta$ linear trajectories will be generated in x-space, in the third case the trajectories become nonlinear.

IV. USING 1-PHASE NONLINEAR PROGRAMMING

Nonlinear target function in the form $t(x)=\sum w_i\, crit_i^p$ under certain conditions can detect nonconvex Pareto fronts. Here the target function is represented by a scaled L_p-norm with weights $w_i \geq 0$, $\sum w_i =1$. Fig. 2 left shows level curve for 2D target function for different p. One has a straight line at p=1, a quadric at p=2, a superquadric at p>2 and a corner at $p=\infty$.

Property: nonlinear target function can be used to detect nonconvex PF, if the curvature of the level curve exceeds the curvature of PF.

Also at higher dimensions, considering the level set (LS) tangent to PF, performing Taylor expansions of LS and PF: $z=u^TMu+o(u^2)$, where u,z are respectively parallel and normal components to a common tangent hyperplane to LS and PF, and requiring $z_{LS}\geq z_{PF}$, one can reformulate the property above as positive definiteness for the difference of curvature matrices M_{LS}-M_{PF}.

Note that L_∞ =max is applicable in any case (minmax method [13]), but the corresponding NLP will be nonsmooth. Practically, one can use large finite p, it is also convenient to normalize y_i in [0,1] and take a log of target function for numerical stability. In this way one achieves so called scalarization of multiobjective optimization, i.e. conversion of multiobjective problem to a single objective one. As a result, the problem becomes solvable with standard NLP-solvers, e.g. ipopt [14]. Here one can impose any additional constraints, e.g. require that $y(x) \leq c$. By putting $c=y_0$ one ensures that the result is better in all criteria than a starting point and finds only a corresponding segment of PF. One can also leave $c=\infty$ and vary w_i to cover the whole PF.

Algorithm NLP1(c):

minimize $t(x)=\log \sum (w_i y_i)^p$, s.t. $y(x) \leq c$.

V. USING 2-PHASE NONLINEAR PROGRAMMING

The following algorithm combines the concepts of linear search from NBI and optimization of nonlinear target function. The first phase performs the linear search in a given direction v in y-space towards PF and the second phase tries to perform further improvement (if possible). The problem is solvable with two calls to ipopt.

Algorithm NLP2:

NLP2.1: maximize t, s.t. $y(x)=y_0+tv$; result y_1;
NLP2.2: call NLP1(y_1); result y_2.

Properties (see Fig. 2 right):

if $y_1 \in$ PF, phase 2 quits immediately;
if $y_1 \in$ non PF boundary, trajectory is bounced to PF.

In NLP2.2 not the whole PF is targeted, but a smaller part ΔPF possessing better criteria than y_1. Here one can use smaller p, while even for too curved PF the result y_2 will be still better than y_0 and y_1.

VI. APPLICATION IN FOCUSED ULTRASONIC THERAPY PLANNING

A generic workflow for ultrasonic therapy simulation has been described in our paper [16]. Numerical simulation with FUSimlib software uses 512 x 512 x 256 voxel grid. Ultrasound has been focused in the center of the target zone for the neutral breath state. The result after 10 seconds of exposure time (200 steps x 0.05sec) has a form of spatial distributions of pressure amplitude, temperature and thermal dose. Fig. 1 top-right shows a typical result for thermal dose on slice 97/256 near the focal point. The frequency of transducer is taken as optimization parameter controlling focused ultrasonic therapy simulation. The other one, initial particle speed, is proportional to an acoustic intensity emitted by the transducer [1]. As optimization objectives the thermal dose inside and outside the target zone have been defined as sums of the thermal dose over corresponding voxels, $\sum$TDin / $\sum$TDout. The variation range of optimization parameters was regularly sampled with 25 simulations, from which 16 fall in the region of interest, shown on Fig. 4 by red points. RBF metamodel constructed on simulation results is used to oversample the region by green points, from which discrete method NDSA selects Pareto front, shown by blue points. We see that Pareto front is of nonconvex type. Magenta lines show application of three continuous methods described above. The trajectories generated by SLP and NLP2 coincide in every detail. Even bouncing from non-PF boundary works similar, although the mechanisms of this bouncing are different. NLP1 with p=8 and w_1=0.01,0.15,0.27,0.5,0.99 produces the other set of trajectories. Table I shows a summary of problem characteristics. SLP provides the best performance for the given application case. On the other hand, NLP is easier for integration with existing scalar solvers. In NLP class, NLP1 is faster than NLP2 for bounced trajectories, otherwise NLP2 is faster. Numerically NLP2 (with small p) is less singular than NLP1 (with large p) and therefore is more robust for detection of strongly curved Pareto fronts.

TABLE I. BI-OBJECTIVE OPTIMIZATION IN FOCUSED ULTRASONIC THERAPY PLANNING, PROBLEM CHARACTERISTICS

Parameter bounds: frequency 0.25…0.75 MHz ini.speed 0.23...0.282 m/s	**Timing per solution** @ 3GHz Intel i7:
Criteria bounds: ∑TDin 0…3000 eq.min ∑ TDout 0…6000 eq.min	SLP 7ms NLP1 16ms NLP2 13ms+12ms

VII. CONCLUSION

Several algorithms of continuous multiobjective optimization applicable for detection of nonconvex Pareto fronts have been discussed: sequential linear programming (SLP), sequential quadratic programming (SQP) and generic 1- or 2-phase nonlinear programming (NLP1,2). Scalarization, i.e. reformulation of the multiobjective optimization problem as constrained optimization with a single objective, allows to employ available NLP solvers for its solution. The algorithms have been applied to realistic test case in focused ultrasonic therapy planning. In the given problem SLP possesses the best performance, while NLP is easier for integration with existing scalar solvers. NLP1 is faster than NLP2 for bounced trajectories, otherwise NLP2 is faster. Numerically NLP2 is less singular than NLP1 and is therefore more robust for detection of strongly curved Pareto fronts. All these optimization methods provide real-time performance necessary for interactive planning of focused ultrasonic therapy.

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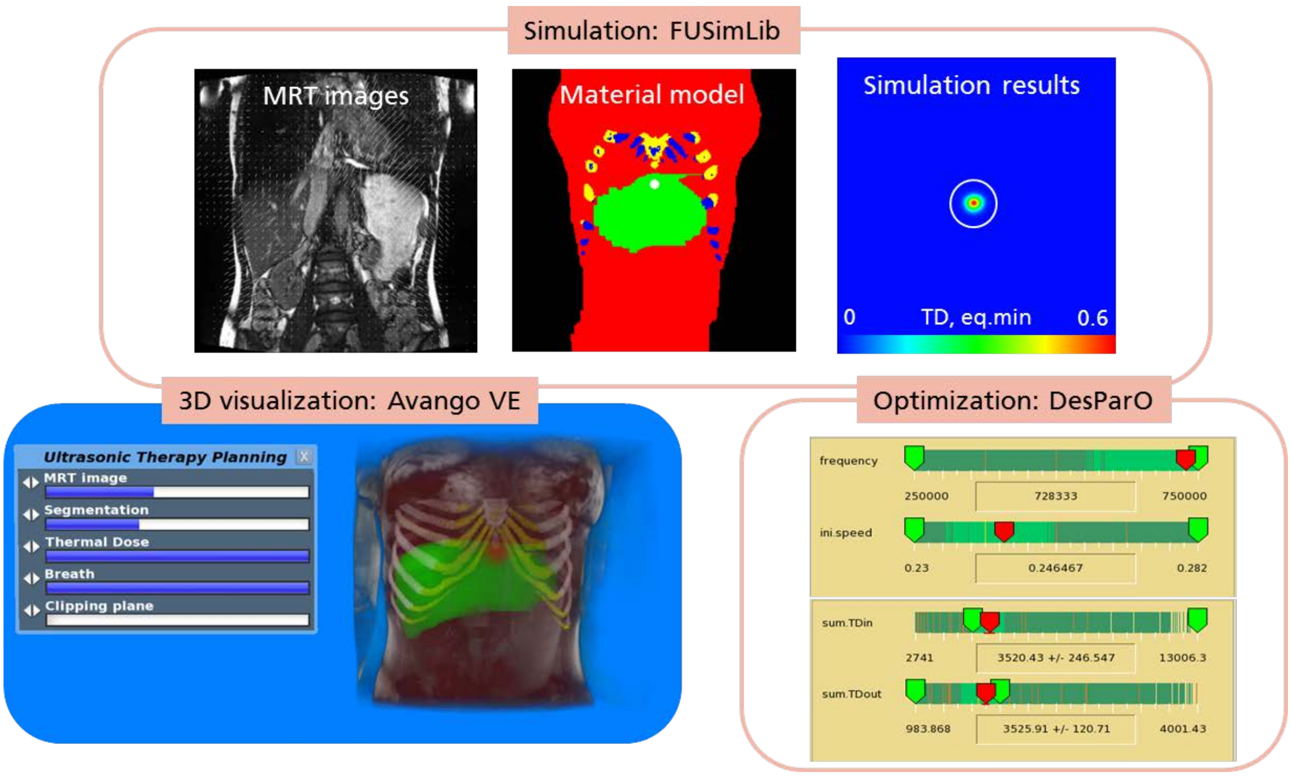

Figure 1. Focused ultrasonic therapy planning and its software components.

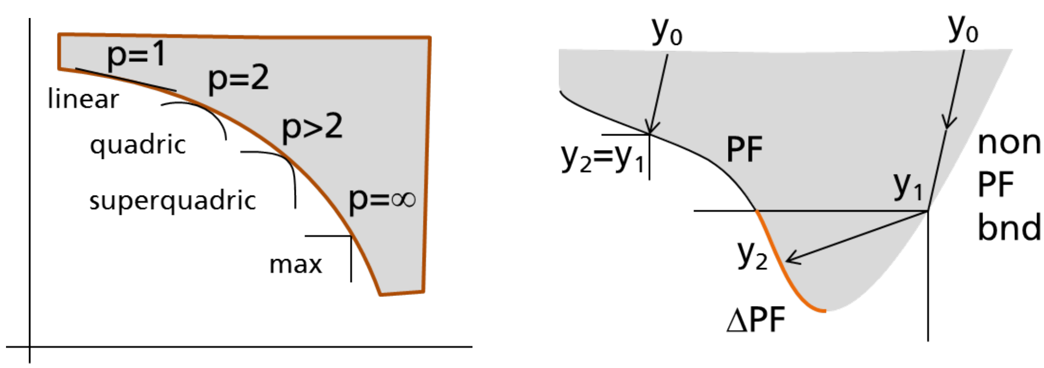

Figure 2. Scalarization of multiobjective optimization problem. On the left: algorithm NLP1; on the right: algorithm NLP2.

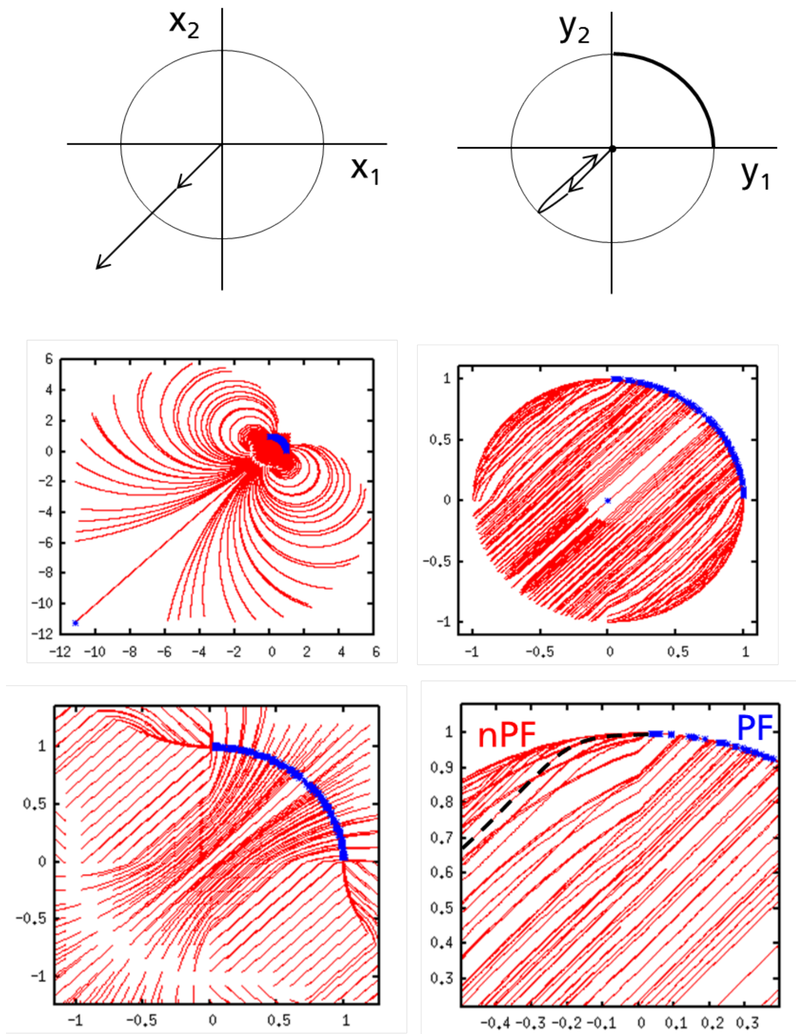

Figure 3. Pareto front detection for 2D fold transform.

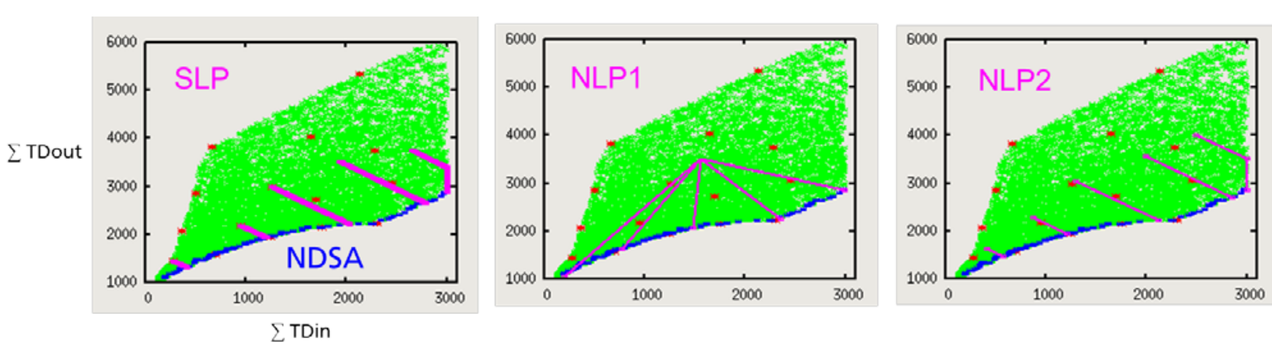

Figure 4. Nonconvex Pareto front in focused ultrasonic therapy planning, comparison of different methods.