Application of Multiobjective Evolutionary Algorithms for Dose Optimization Problems in Brachytherapy

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Abstract

In High Dose Rate (HDR) brachytherapy the conventional dose optimization algorithms consider the multiple objectives in form of an aggregate function which combines individual objectives into a single utility value. As a result, the optimization problem becomes single objective, prior to optimization. Up to 300 parameters must be optimized satisfying objectives which are often competing. We use multiobjective dose optimization methods where the objectives are expressed in terms of quantities derived from dose-volume histograms or in terms of statistical parameters of dose distributions from a small number of sampling points. For the last approach we compare the optimization results of evolutionary multiobjective algorithms with deterministic optimization methods. The deterministic algorithms are very efficient and produce the best results. The performance of the multiobjective evolutionary algorithms is improved if a small part of the population is initialized by deterministic algorithms.

1 Introduction

High dose rate brachytherapy is a treatment method for cancer where empty catheters are inserted within the tumor volume. Once the correct position of these catheters is verified, a single ^{192}Ir source is moved inside the catheters at discrete positions (dwell positions) using a computer controlled machine. The problem that we consider is the determination of the n dwell times (which sometimes are called as well dwell position weights or simply weights) for which the source is at rest and delivers radiation at each of the n dwell positions, resulting in a three-dimensional dose distribution which fulfills the defined quality criteria. In modern brachytherapy, the dose distribution has to be evaluated with respect to the irradiated normal tissues and the Planning Target Volume (PTV) which includes besides the Gross Tumor Volume (GTV) an additional margin accounting for position inaccuracies, patient movements, etc. Additionally, for all critical structures, either located within the PTV or in its immediate vicinity or otherwise within the body contour, the dose should be smaller than a critical dose D_{crit}. In practice it is difficult, if not impossible to meet all these objectives. Usually, the above mentioned objectives are mathematically quantified separately, using different objective functions and then added together in various proportions to define the overall treatment objective function [1],[2].

The number of source positions varies from 20 to 300. It is therefore a high dimensional problem with competing objectives. The use of a single weighted sum leads to information loss and is not generally to be recommended, especially for non convex problems and for those cases where

objectives have not the same dimensions and in addition maybe competing. An understanding of which objectives are competing or non-competing is valuable information. We therefore use multiobjective evolutionary algorithms in HDR brachytherapy. One algorithm is based on the optimization of dose-volume histograms (DVH), which describes the distribution of the dose within an object, or from these derived distributions. These distributions are evaluated for the PTV, the surrounding tissue and organs at risk from a set of up to 100000 sampling points [3]. The calculation of the DVH requires a considerable amount of time and for implants with 300 sources the optimization requires a few hours. Another limitation of this method is that a comparison with deterministic algorithms is not possible. We have therefore considered the optimization of the dose distribution using as objectives the variance of the dose distribution on the PTV surface and within the PTV obtained from a set of 1500-4000 sampling points. These functions are convex and a unique global minimum exists.

In the past comparisons of the effectiveness of evolutionary algorithms have been made with either other evolutionary algorithms [4] or with manually optimized plans [1],[2]. We have compared the Pareto fronts obtained by multiobjective evolutionary algorithms with the Pareto fronts obtained by a weighted sum approach using deterministic optimization methods such as quasi-Newton algorithms and Powells modified conjugate gradient algorithm which does not requires derivatives of the objective function [5].

2 Methods

2.1 Calculation of the Dose Rate

The dose rate around each of the small cylindrical shaped sources is dominated by the $1/r^2$ term with modifications due to absorption and scattering in the surrounding material. The dose value $d(r)$ at $r=(x, y, z)$ is:

$$d(x) = \sum_{i=1}^{N_S} w_i K(r - r_i) \qquad (1)$$

In (1) r_i is the position of the i^{th} source and N_s the total number of sources. $K(r-r_i)$ is the dosimetric kernel describing the dose rate per unit source strength at r from a source positioned at r_i. The dwell position weight $w_i = S_k \cdot t_i$ is proportional to the strength S_k of the of the single stepping source, where t_i is the dwell time of the i^{th} source dwell position [6]. Because of the high dose gradients a dose specification at a single point inside the PTV is not possible in interstitial brachytherapy. For this reason we use as a reference dose D_{ref} the average dose value at the PTV surface.

2.2 Dose-Volume Histogram Based Optimization Using the Conformal Index

In the paper of Baltas et al. [7] a conformal Index (COIN) was proposed as a measure of implant quality and dose specification in brachytherapy. This index takes into account patient anatomy, both of the tumor and normal tissues and organs, see Fig. 1.

COIN is defined as:

$$\text{COIN} = c_1 c_2 \qquad (2)$$

where $c_1 = V_{ref}^{PTV}/V_{PTV}$ and $c_2 = V_{ref}^{PTV} / V_{ref}$. The coefficient c_1 is the fraction of the PTV, V_{ref}^{PTV}, that is enclosed by D_{ref} and is a measure of how accurately the PTV is covered by D_{ref}. The coefficient c_2 is the fraction of the volume of the reference dose, V_{ref}, that is covered by PTV. It is also a measure of how much normal tissue outside the PTV is covered by D_{ref}. COIN can be calculated from the cumulative DVHs of the PTV and the body at the reference dose D_{ref} i.e. $DVH_{PTV}(D_{ref})$ and $DVH_{body}(D_{ref})$ respectively:

$$COIN = V_{PTV} * DVH_{PTV}(D_{ref})_2 \quad / 100\ V_{body} * DVH_{body}(D_{ref}) \qquad (3)$$

V_{body}, V_{PTV} are the volumes of the body and the PTV, respectively. We describe the dependence of the conformal index COIN on the choice of the reference dose value as the COIN distribution, see Fig. 2(b). Usually the dose values are normalized to D_{ref} and are given either as fractions or percentages of D_{ref}.

The "ideal" dose distribution is characterized by the following:

- $c_1=c_2=1$ i.e. COIN=1 at $D=D_{ref}$, which means that the reference dose value isodose 3D envelope is identical with the PTV.
- For $D < D_{ref}$, an extremely rapid fall-off of the COIN value which corresponds to a rapid fall-off of the dose outside the PTV (normal tissues).
- $COIN \approx 0$ for $D > D_{ref}$, that means that there are negligible volumes with dose values higher than $D < D_{ref}$.

The cumulative dose volume histograms of the PTV and the body for a rib implant is shown in Fig. 2(a). Due the rapid decrease of the DVH of the body a large number of sampling points is necessary in order to calculate with a high accuracy the DVH, the COIN distribution and the COIN integral at dose values close to the reference dose value and above. The COIN distribution from the DVHs of Fig. 2(a) and the COIN integral is shown in Fig. 2(b).

2.3 Dose Statistics Based Optimization

The DVH based optimization method requires a large number of sampling points for the computation of the histograms and the COIN distribution and therefore is computational expensive. We have developed a stratified sampling approach where the sampling points are non uniform distributed and which reduces the number of required sampling points by a factor of 5-10. Even then for implants with 200-300 sources the optimization time can reach 1-2 hours. A comparison of the performance with deterministic and gradient based algorithms is not practical or not even possible. Therefore we consider another set of two objectives: For the conformity objective we use the variance f_S of the dose distribution of sampling points uniformly distributed on the PTV. In order to avoid excessive high dose values inside the PTV we require a small as possible dose distribution variance f_V inside the PTV. Due to the source characteristics these two objectives are competing. We use normalized variances for the two objectives:

$$f = \frac{1}{m^2} \sum_{i=1}^{N} (d_i - m)^2 \qquad (4)$$

Where m is the average dose value and N the corresponding number of sampling points.

2.4 Multiobjective Optimization with Deterministic Algorithms

These objectives allow us to use deterministic gradient based algorithms. We use a weighted sum approach for the multiobjective optimization, where for a set of weights for the volume and surface variance we perform a single objective optimization of f_w :

$$f_W = w_S f_S + w_V f_V \qquad (5)$$

where $w_S, w_V \geq 0$ are the surface and volume importance factors, respectively and $w_S + w_V = 1$. We used 21 optimization runs where w_S varied from 0 to 1 in steps of 0.05 to determine the shape of the trade-off curve. A problem in using deterministic optimization methods is that the solution contains a large number of dwell weights with negative values. This is a non physical solution. In the past either constrained optimization methods were used or a correction was applied by setting to 0 all negative weights in each optimization step. A constrained optimization method increases the number of parameters by a factor of two. The correction method for the negative weights reduces the quality of the optimization results. We use a simple technique by replacing the decision variables, the weights w_k, with the parameters $w'_k = w_k^{1/2}$. Using this mapping technique we avoid non feasible solutions. For this unconstrained optimization we use the Polak-Ribiere variant of Fletcher-Reeves algorithm or the Broyden-Fletcher-Goldfarb-Shanno quasi-Newton based algorithm [5]. These require the first derivative of the objective function with respect to the decision variables to be calculated. The derivative of the normalized variance f used by the gradient based optimization methods is:

$$\frac{\partial f}{\partial w'_k} = \frac{2}{N m^3} \sum_{i=1}^{N} (d_i - m) \left[m \frac{\partial d_i}{\partial w'_k} - d_i \frac{\partial m}{\partial w'_k} \right] \qquad (6)$$

As a gradient free method we used the modified Powell method of Numerical Recipes [5] .

2.5 Multiobjective Optimization with evolutionary Algorithms

The population of our multiobjective evolutionary algorithm consists of strings storing a set of weights for each source dwell position. The weights are initially produced randomly distributed in the interval [0, 1]. A part of the population can be initialized, if this is possible, by solutions of deterministic algorithms.

Three selection mechanism can be used. The niched Pareto algorithm (NPGA) proposed by Horn and Nafpliotis [8], the strength evolutionary approach algorithm (SPEA) by Zitzler and Thiele [9] and the non dominated ranking algorithm (NRGA) by Fonseca and Fleming [10],[11] .

After a new population is formed, the strings of randomly selected pairs undergo a crossover operation with a probability P_c and mutation with a probability P_m. We have found that P_c must

be larger than 0.7 and P_m should be smaller than 0.1. The size of the population should be larger than 50. Various crossover types can be selected such as single point, two point, and arithmetic crossover. For the mutation operation also we have used various forms: uniform or non-uniform mutation. We use a real representation for the gene values. A detailed description of the genetic operators is given in reference [12].

For the NPGA algorithm we use a tournament selection, the tournament population size is a free parameter and can be used for the modification of the selective pressure. Tests have shown that it should be normally 10 % of the population size. For much smaller values the genetic algorithm is sensitive to fluctuations, while much larger values can lead to a premature convergence. We applied special genetic operators for decision variables as described by Michalewicz [13]. Some of them offer the possibility for a better performance of the genetic algorithms in the late stage of the optimization process. For NPGA we use a sharing mechanism described by S. Deb [14]. The sharing parameter σ_{share} is given by:

$$s_{share} \approx \sqrt[P]{q} \qquad (7)$$

where q is the desired number of distinct Pareto-optimal solutions and P is the number of variables in the problem.

Selecting the Solution from the Pareto Set

After the last generation is processed by the SPEA, NRGA or NPGA algorithm, members of the population are expected to be close to the Pareto frontier. A member of the non dominated set is selected which has a minimum Euclidean distance to the ideal optimum. The ideal point is defined by the minimum values (f_1^{min}, f_2^{min}) of each objective function. The distance is calculated by normalizing each objective to a maximum value of 1 using the corresponding largest objective value found in the population. This member is presented as the solution of the optimization process. Additionally members are selected each with the best result in each objective. A list is produced with the objective values for all the members of the Pareto set. Additionally the user can examine the dose distributions and the dose-volume histogram and isodose contours of every member of the population. Based on this information of the trade-off surface of the various objectives a decision maker can select the best result. In our current implementation each objective has equal priority.

3 Results

The dose variances are calculated from 1000-4000 quasi-randomly distributed sampling points. For the COIN based optimitation ≈ 100000 points are generated. The distances of these points to each source dwell position r, more precisely the inverse square distances $1/r^2$, are stored for speed maximization in look-up tables. We assume a invariant kernel $K(r)= 1/r^2$ and ignore any spatial anisotropy, namely attenuation and scattering effect. This dosimetric simplification has no measurable influence on the results of the optimization.

All calculations presented in our study have been made by using for the mutation probability P_m a value of 0.0065 and for the crossover probability P_c a value of 0.85. Furthermore a uniform mutation option has been selected and a two point crossover has been used. The selection of a two point crossover means that the string representation of a member is cut at two random

positions and the two end parts are interchanged. This increases the efficiency of the exploitation [15].

The optimization time depends mainly on the number of dwell positions and the population size. For 200 dwell positions and up to 200 generations it can take 1 hour with an Intel Pentium III 700 MHz processor with 512 MB RAM.

The flowchart for the COIN based optimization algorithm is shown in Fig. 3. For each member of the population for a given generation a renormalization is carried out according to the resulting COIN distribution, so that the maximum COIN value is observed at $D= D_{ref}$ [7]. The dose prescription is realized at the D_{ref}, the isodose value resulting in the maximal conformity. This results generally in mean normalized dose values at the surface of PTV different from 1.0.

The multiobjective genetic algorithm, which uses dose-volume based constraints, produces equivalent or even better results than algorithms which were based on phenomenological methods and used in the majority of treatment planning systems [16],[17],[18].

As an example in Fig. 4 the multiobjective genetic algorithm provides a solution with a more homogeneous dose distribution inside the PTV than by conventional optimization algorithms of a treatment planning system. Due to the large computational time for the COIN based optimization we used only the NPGA algorithm.

For the variance based objectives we used 22 different implant cases from various anatomic regions. For these implants different number of catheters were used and their topology differed from case to case. The study aimed to assess the dose homogeneity and conformity and to determine if a common set of importance factors exists, allowing a single objective function to be used with these weights.

An example of the geometry of a PTV is shown in Fig. 5(a) including the catheters, the source dwell positions and the sampling points on the PTV surface which define the surface variance. In Fig. 5(b) the isosurface for the prescription dose is shown, which should have the same shape as the PTV.

The deterministic gradient based algorithms are very effective in generating the Pareto front using a summed weights approach. Powells algorithm which does not require derivatives is efficient only for implants with a small number of sources. For implants with 250-300 sources the optimization time can reach a few hours for a single objective run, whereas the gradient based algorithms require only 1-2 minutes. Gradient based algorithms are limited by the fact that they can be trapped in local minima, or that non convex regions are not accessible using the weighted sum method [19].

From the evolutionary algorithms SPEA has been found to produce the best results, since it applies an elitism and sharing mechanism. Therefore the Pareto fronts are more uniformly distributed as compared with NPGA. For implants with a small number of sources SPEA generated solutions close to the Pareto sets found by the deterministic algorithms. For implants with many sources the genetic algorithms used converge in some cases to a Pareto set which was far away from the true Pareto set. Such an example for an implant with 215 source dwell

positions is shown in Fig. 6. The SPEA algorithm converges after 200 generations to a Pareto front which is very small and far from the Pareto set generated by the gradient based algorithms. The optimization path is shown for a set of importance factors f_V, f_S for the Polak-Ribiere algorithm. After 10 iterations a point on the Pareto front is reached.

Using random sets of decision variables we have found for this example that the number of function evaluations required by a random search method to obtain points on the Pareto front is larger than 10^{30} [12]. A random search would require 10^{10} times more function evaluations to generate points on the Pareto set found by the SPEA algorithm without initialization. Even with this performance the SPEA algorithm is not able to produce points on the Pareto front found by the deterministic methods. Using a few members initialized by the gradient based algorithm the multiobjective evolutionary algorithms, especially SPEA reproduced the Pareto fronts obtained by the deterministic algorithms, see Fig. 6. For a more detailed comparison of the deterministic and evolutionary algorithms see reference [12].

Fig. 7 shows the Pareto fronts for the 22 implants. For some implants a improvement in dose homogeneity is possible without reducing the COIN value which is correlated with the surface variance, while for some implants there is a strong trade off between these two objectives. Therefore a multiobjective optimization is essential for the dose optimization problem in brachytherapy.

4 Conclusions

We used for the first time multiobjective evolutionary anatomy based dose optimization algorithms in HDR brachytherapy [16]. For the COIN-based objectives we have found that multiobjective evolutionary algorithms produced solutions which are better than by conventional algorithms in treatment planning systems which use deterministic algorithms and catheter-oriented objectives. They also have the problem with infeasible negative weights which they avoid by a repair mechanism or by using special constraints to the objective functions in order to reduce their numbers and the degree of the violation.

The results of various algorithms for the variance based objectives have been compared using a representative set of 22 implants encountered in clinical practice. We have limited our study to cases where no critical structures are considered. Trade-off surfaces which reveal the nature of the multiobjective problem of the dose optimization in brachytherapy have been obtained. Due to the variety of the trade-off surfaces found, which depends on the implant and complex catheter geometry, no common set of optimal importance factors exists. Therefore it is useful to determine the Pareto front and then to select a solution according to its characteristics. Pareto sets have been obtained by a deterministic unconstrained optimization method using a simple mapping technique which transforms the linear into a quadratic optimization problem and removes infeasible solutions with negative dwell position weights. The gradient based algorithms, if they can be used, are very effective because they converge very fast and generate the Pareto fronts which in most cases are much better than the Pareto front obtained by evolutionary multiobjective algorithms.

If the number of objectives increases then the number of combinations using a weighted sum approach with deterministic algorithms increases. Deterministic methods are not efficient for non analytic complex objectives such as used by the COIN based method. When more objectives

are included then a non convex feasible space could be the result [20]. A combination of deterministic and evolutionary multiobjective algorithms seems to be the best choice for a robust and efficient multiobjective dose optimization in HDR brachytherapy. The targets of the dose optimization cannot be expressed uniquely by a single set of objective functions. This is because conformity and homogeneity can be expressed with various functional forms and for the complex geometry of the PTV and the variety of topological configurations it is not known which set is the best. Is the COIN based dose optimization approach better than the dose-statistics approach using variances and if yes how much better?

We are currently studying for various sets of objectives the Pareto fronts using multiobjective evolutionary algorithms and if possible in combination with deterministic algorithms. We expect to understand their limitations and their robustness and performance for the complex problem of the dose-optimization in brachytherapy.

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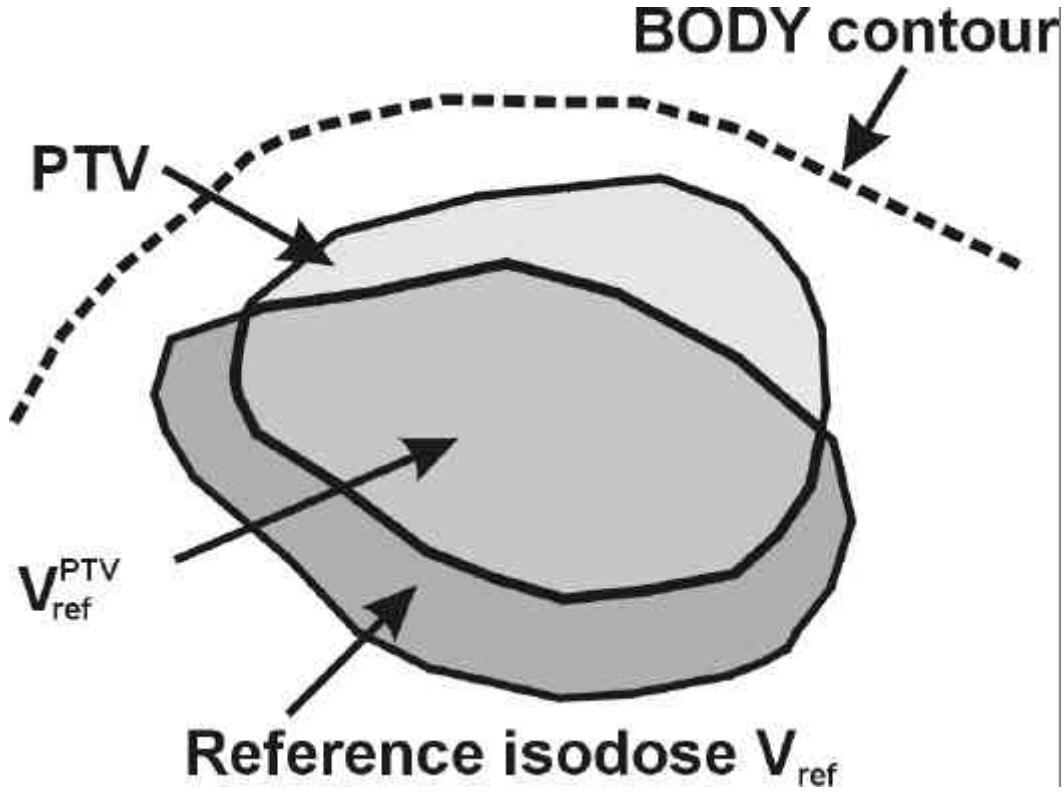

Fig. 1. Two-dimensional schematic diagram of the COIN=c_1c_2 based optimization. The coefficients c_1 and c_2 consider the coverage of the PTV by the isosurface with the prescription dose D_{ref} and parts of the tissue surrounding the PTV.

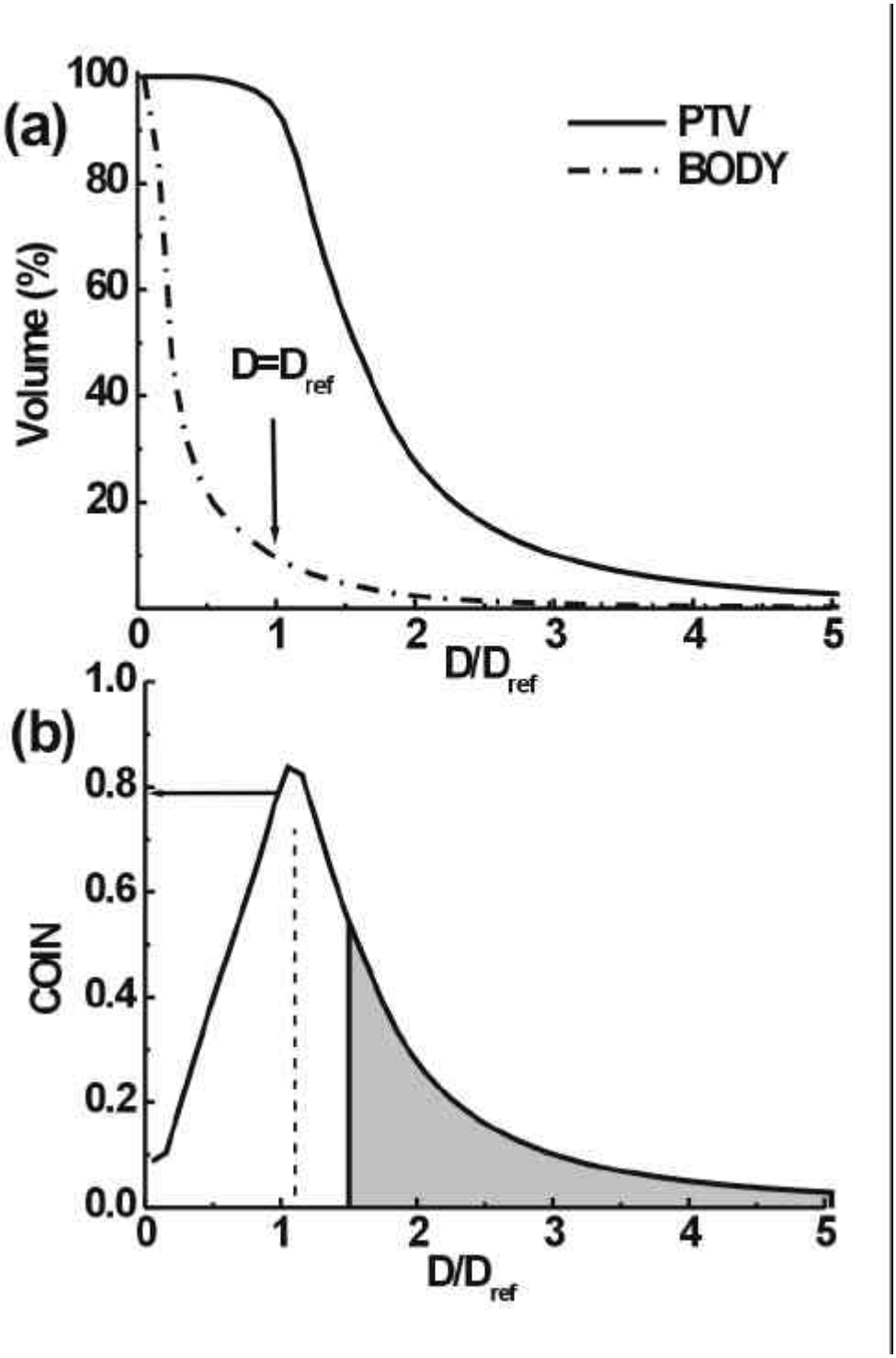

Fig. 2. (a)Dose-volume histograms of the PTV and the body as a function of dose. (b)The corresponding COIN distribution. The shaded area to the right of D/D_{ref} =1.5 is the COIN integral. The objectives are maximum COIN value at $D=D_{ref}$ and minimum COIN integral for the avoidance of high dose values in the PTV and the surrounding tissue.

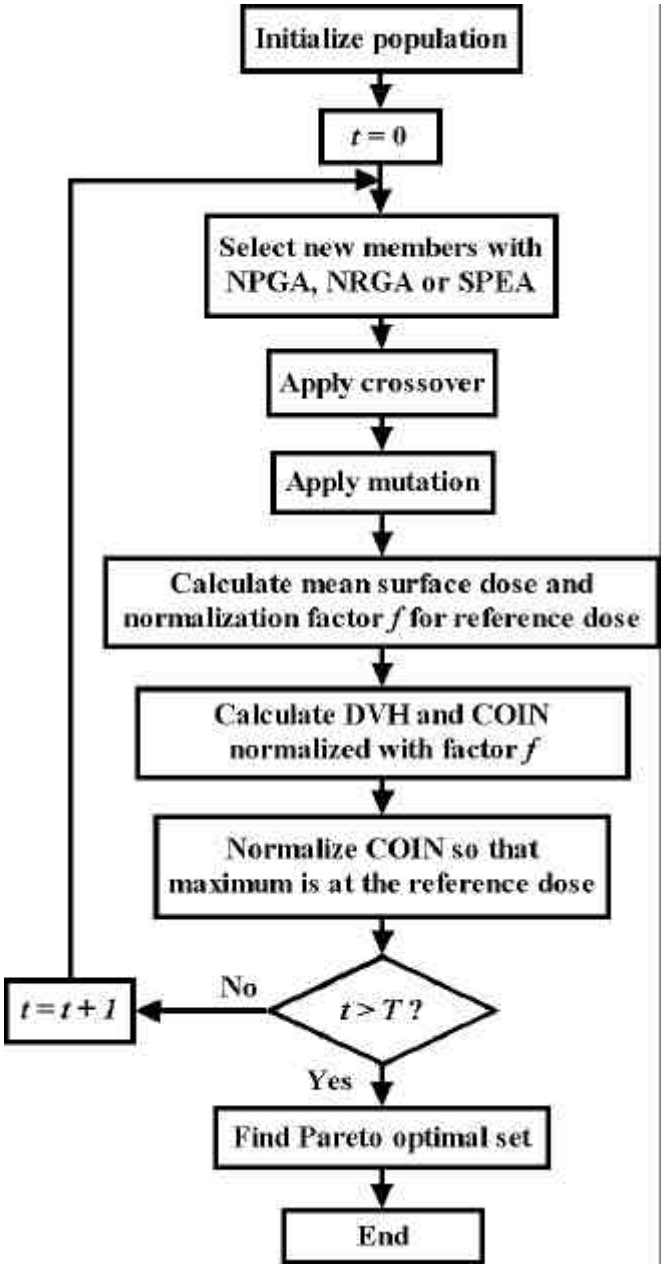

Fig. 3. Flow diagram for the dose-volume histogram based multiobjective genetic algorithm.

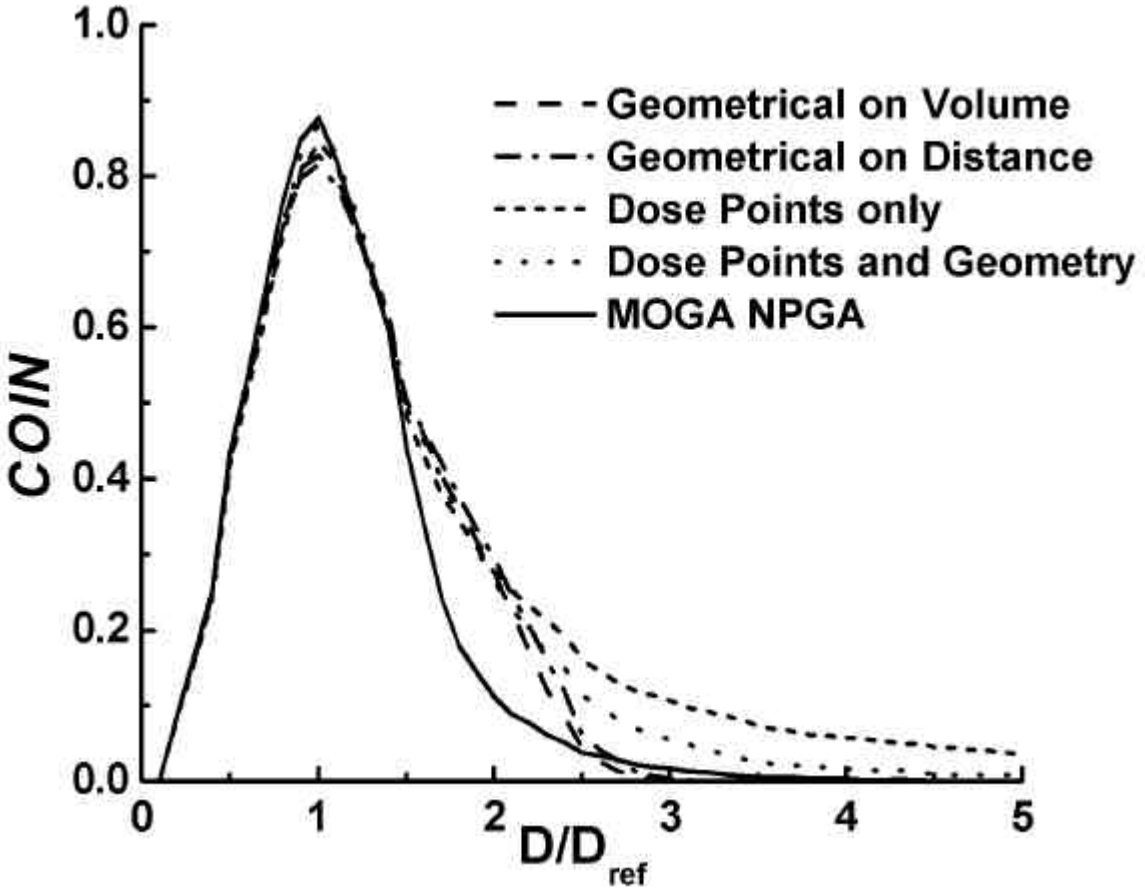

Fig. 4. Comparison of the COIN distributions for a breast implant from the multiobjective genetic algorithm and four conventional single objective algorithms.

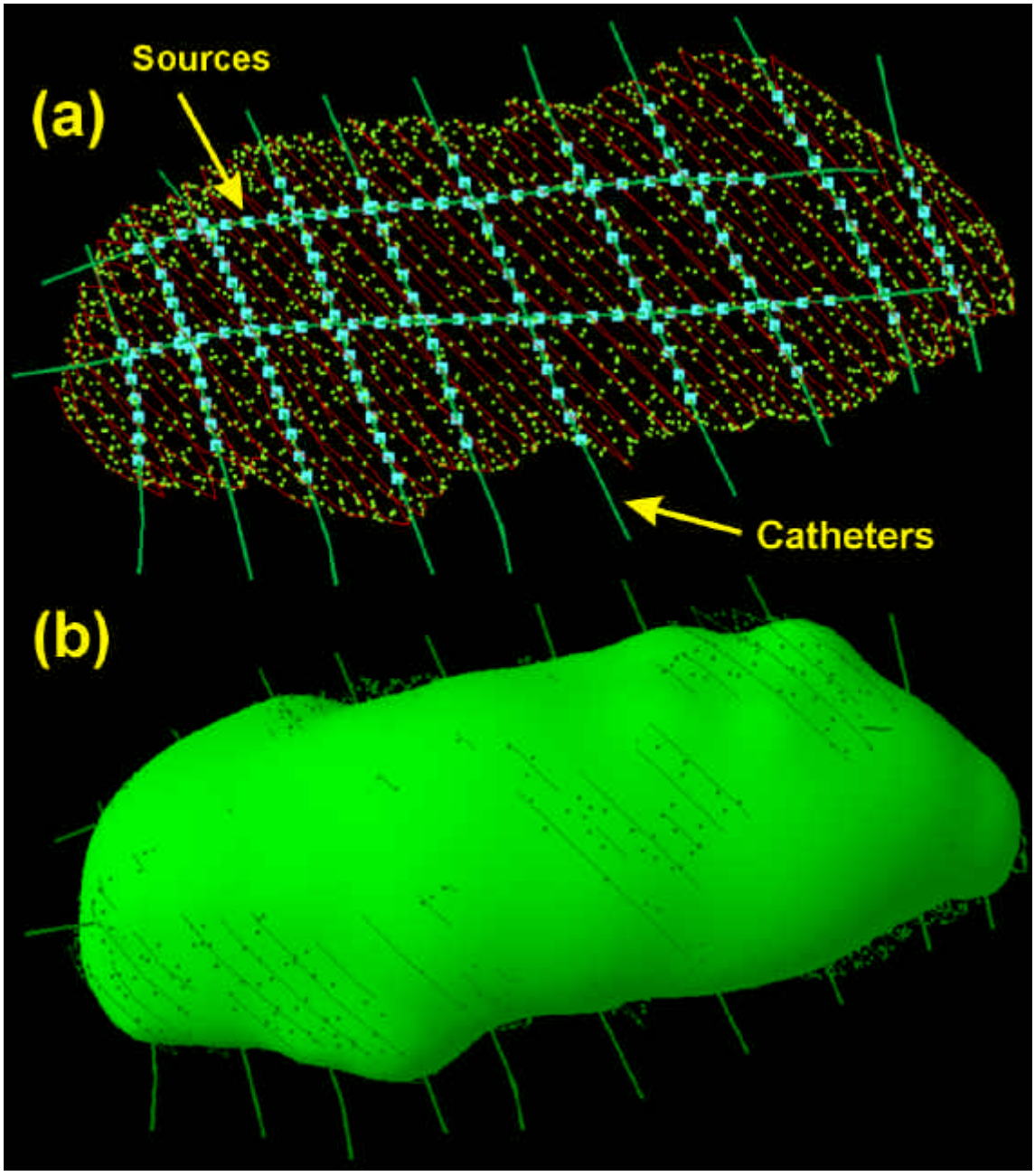

Fig. 5. Contours of a rib implant with the catheters and the source dwell positions. On the PTV surface sampling points are shown at which the dose is calculated b) the dose isosurface obtained from the dose optimization.

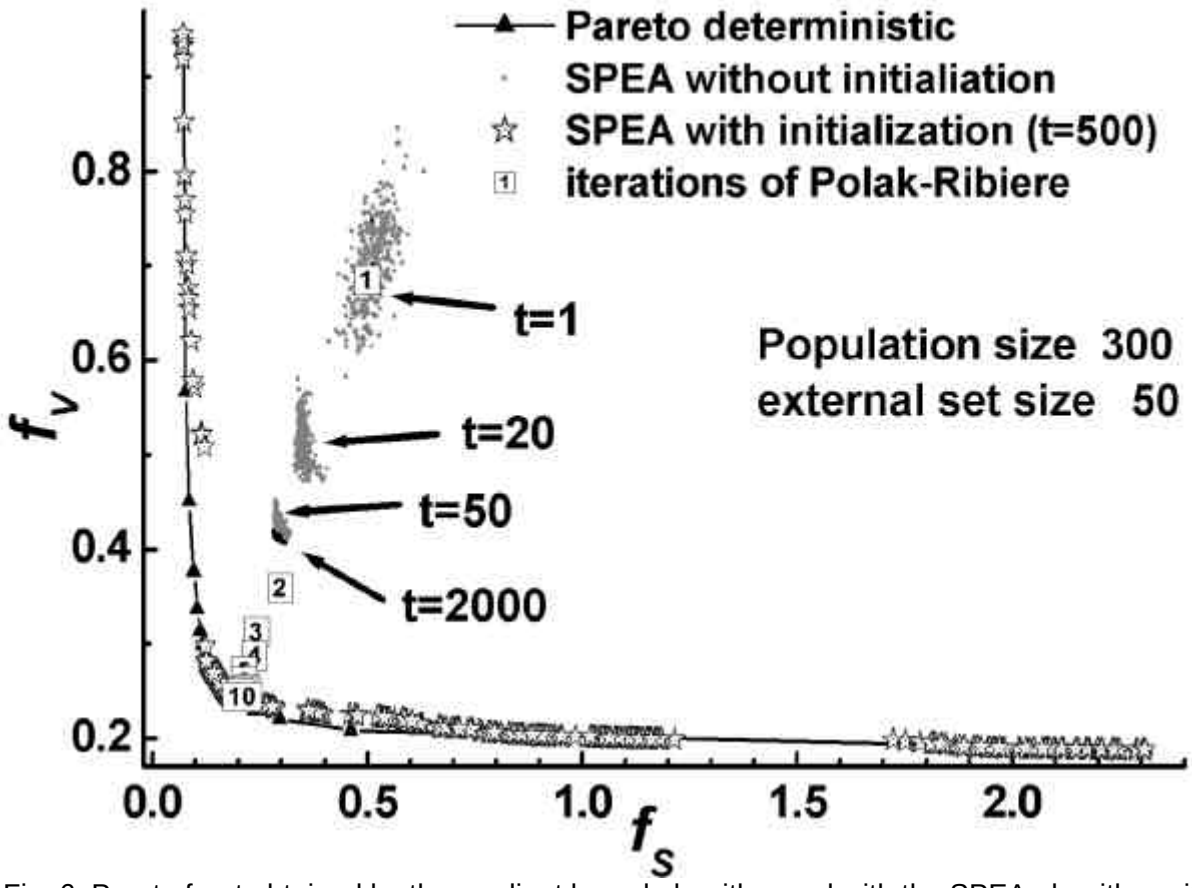

Fig. 6. Pareto front obtained by the gradient based algorithm and with the SPEA algorithm with and without initialization.

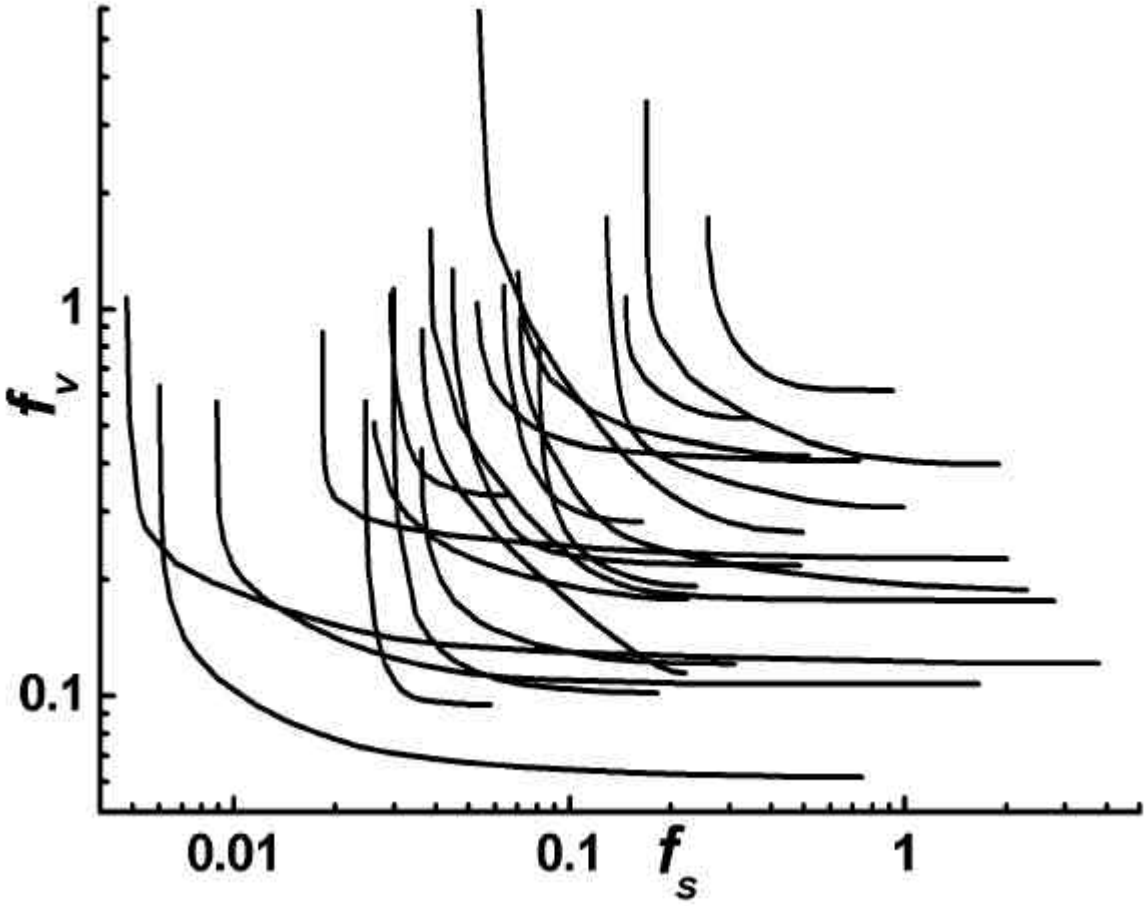

Fig. 7. Pareto fronts obtained by the gradient based algorithm for 22 implants. The variety shows that a single objective optimization with constant importance factors does not give always a good result.