Real-time DMLC IMRT delivery for mobile and deforming targets

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In numerous cases of radiotherapy delivery to moving targets, simplifying assumptions of identical pattern of motions of tissue for each fraction are not satisfied. Therefore, algorithms capable to respond in real time to motions of target registered at treatment should be developed to improve the precision of radiation intensity delivery. The DMLC delivery of predetermined intensity maps to moving and deforming targets in real time is developed in this paper. Algorithms are constructed so that constraints on maximum admissible speed of leaves are preserved during delivery. A sequence of examples is presented to illustrate behavior of leaf trajectories for representative cases of [dynamic multileaf collimator] (DMLC) [intensity modulated radiation therapy] (IMRT) real-time delivery. The examples presented show real-time deliveries to targets moving as rigid bodies and targets deforming uniformly over their volumes. Examples are admitting random perturbations of predefined target motions that are time dependent only, i.e., target motion perturbations are identical for all target points. © 2005 American Association of Physicists in Medicine. [DOI: 10.1118/1.1987967]

I. INTRODUCTION

Image-guided radiation therapy (IGRT) in real time attracts considerable attention recently.1–6 IGRT in real time requires integration of imaging techniques (image guidance—IG) and development of special tools and algorithms in radiation therapy (RT) delivery. IG investigations are directed towards fast image data registration and modeling of tissue motions. Modeling of tissue motions includes recognition of organs’ (tumors’) surfaces as well as description of these surfaces’ translations, rotations, and deformations with time. The aim is to learn as much as possible about various organ and tumor motions that take place between treatments as well as during the time of treatment itself. IG investigations of organ motion during treatment delivery (real-time imaging) have attracted, so far, more attention than developments of special tools and algorithms capable of responding in real time to organ/target motion. A few examples of investigations in the area of tool developments for IGRT real-time delivery7–11 are associated with the Cyber Knife®. In the Cyber Knife® approach the fixed aperture of the beam is directed towards the tumor by the robotic arm, and it tracks moving target (organ) in response to the real-time registered image of patient’s internal structures.5 However, no analysis of real-time MLC delivery of IGRT for intensity modulated radiation therapy (IMRT) has been discussed in the literature so far. This paper intends to initiate investigations of real-time IG IMRT with MLC. Methods and results of real-time DMLC IGRT delivery will be discussed in this article in terms of solutions for leaf trajectories for each leaf pair independently. Thus, each time the discussion in the paper refers to the motion of the leading or following leaf, it means that leaves of the same pair are being considered.

Studies in this paper continue on earlier developed models of motions of MLC collimators that deliver IMRT treatments to moving and deforming targets.12–15 These earlier models relied, however, on the assumption that motions of targets are known before treatment is initiated. Thus, the main assumption of these earlier models was that the motion of the target at the time of delivery does not depart from the predefined dynamical behavior of the target. Studies in this paper, on the other hand, assume realistically that only general features of target motions can be known before treatment is initiated, and that the actual details of target motions at delivery depart from the predetermined dynamical behavior of the target that has been registered before treatment, presumably during the time of patient CT simulation.

To appreciate the nature of the problem under consideration, it is worth-while to recognize that shaping the intensity $I(x)$ during IMRT delivery results from accumulation of photon radiation passing over each point of the beam field between the moment of opening and the moment of closing of this given point by leaves of each MLC pair. These moments of opening and closing of the radiation field over different points of the target are defined by correlated motions of leading and following leaves.12–15 If the motion of the target is known a priori for all moments for which trajectories of leaf evolutions are to be determined, it is possible to choose, by developing and solving appropriate differential equations, unique optimal trajectories for leaf motions.12–14 This is achieved, by selecting, from the set of all admissible leaf motions that deliver the predetermined intensity pattern and satisfy also constraints imposed on leaf maximal velocities, those leaf trajectories that minimize the time of treatment delivery. The a priori knowledge of the target motion at time of treatment makes possible the definition of differential equations that determine leaf trajectories optimizing IMRT delivery. This is valid for cases when intensity is delivered over targets that move as rigid bodies,12,13 as well as for
cases when targets experience deformations during their evolutions.\textsuperscript{14}

In contrast, in the real-time data setting approach the motion of the target is unknown for all future moments $m$ when the leading (right) leaf is moving over any particular point $x$ of the target. Let us notice that the variable $m$ is understood in this paper as time expressed in MU, and that this variable parametrizes the motion of the target and the motion of leaf trajectories (see Refs. 7–9 for more detailed discussion of advantages of utilizing MU as a time-enumenrating parameter). Thus, the attempt to maximize the speed of the leading leaf at moment $m$ over point $x$ is futile—the maximum speed of the leading leaf over $x$ depends on the unknown speed of the target at the moment $m+I(x)$ when the following leaf moves over $x$ and is thus not defined by optimality itself. Thus, we notice that not all goals that are reachable in a priori data setting for moving targets can be attained in a real-time data setting delivery. In real-time data setting at least one of the goals

(1) delivering the given intensity;
(2) minimizing the time of delivery; or
(3) preserving the maximum speed of leaf motion to below the speed of $v_{\text{max}}$.

has to be compromised. As goals (1) and (3) above constitute indispensable conditions for clinically acceptable DMLC IMRT delivery, the crucial question for the problem under consideration is, Is delivery of DMLC IMRT possible in real-time data setting if goal (2) of the minimization of the time of delivery is sacrificed? Fortunately, the answer to this question is yes. This paper shows how this goal can be achieved.

II. METHODS

A. Optimal leaf trajectories for a priori target motion data setting and over-restrictive constraints

Let the predefined one-dimensional deforming motion of the target be given as a function $y_T$ that assigns to each internal point of the target $(x)$ and each moment of time ($m$) spatial coordinate $y$ in the laboratory frame of reference.\textsuperscript{14} Thus, $y_T$ is a mapping from a planar domain $[x_0,x_f] \times [0,M]$ into an interval $[y_0,y_f]$ that can be represented as $y_T : [x_0,x_f] \times [0,M] \rightarrow [y_0,y_f]$ or as $y=y_T(x,m)$. Here, $x_0$ and $x_f$ denote coordinates of the left and of the right edge of the target (at the moment of target motion equilibrium), $[0,M]$ is the interval over which the target evolution is defined, $y_0$ is the coordinate of the minimal value for $x_0$, and $y_f$ is the coordinate of the maximal value for $x_f$, during target motion evolution. The velocity of a point $x$ of the target at instance $m$ is thus a time derivative of trajectory $y_T(x,m)$.

This quantity can be interpreted as a velocity of local translation of a point $x$ in the target, and it may be denoted by $v_T(m,x)$; thus, $v_T(m,x)=[dy_T(x,m)]/dm$. It is assumed in this paper that velocities $v_T(m,x)$ satisfy, uniformly with respect to all $m$ and $x$, the constraint $-v_{\text{max}} \leq v_T(m,x) \leq v_{\text{max}}$. Similarly, the rate of target's local deformation, defined as the spatial derivative of trajectory $y_T(m,x)$, is also a function of time $m$ and target point position $x$. It is denoted by $d_T(m,x)$ and so we have $d_T(m,x)=[dy_T(m,x)]/dx>0$.\textsuperscript{14} For convenience and more compact notation of future formulas, we introduce also the following notation. A function $b(m,x)$ is defined as the ratio of the target’s local deformation at times $m$ and $m+I(x)$ when leading and following leaves pass over point $x$ of the target. Thus, $b(m,x)$ can be written as

$$b(m,x)=[d_T[m+I(x),x]]/[d_T[m,x]]>0.$$  

The right (leading) and left (following) leaf trajectories, observed in the laboratory frame of reference, are denoted appropriately by $y_L(m)$ and $y_R(m)$. If the right (leading) leaf trajectory $y_R(m)$ reaches coordinate $y$ at instance $m$ in the laboratory frame of reference, while moving over point $x$ of the target, we register this event as $y=y_R(x,m)$ and denote velocity of the leading leaf coinciding with this event as $v_R(m,x)$, where $v_R(m,x)=[dy_R(m,x)]/dm$. In a similar fashion, if the left (following) leaf trajectory $y_L(m)$ reaches at instance $m+I(x)$ coordinate $y$ in the laboratory frame of reference, while moving over point $x$ of the target, we register this event as $y=y_L(m+I(x),x)$ and denote velocity of following leaf (in laboratory frame of reference) coinciding with this event as $v_L(m+I(x),x)$, where $v_L(m+I(x),x)=[dy_L(m+I(x),x)]/dm$.

The above-developed notation for parameters describing deforming motion of the target as well as for parameters characterizing motions of MLC leaves allows us to recall and interpret the relationship

$$v_L[m+I(x),x] = \frac{b(m,x) \cdot [v_R(m,x) - v_L(m,x)]}{1 + (d_T)^{-1}(m,x) \cdot I'(x) \cdot [v_R(m,x) - v_L(m,x)]} + v_L[m+I(x),x]$$

(see Ref. 14 for the derivation of this formula) between leading leaf velocity $v_R$ at $m$ over $x$ and following leaf velocity $v_L$ at $m+I(x)$ over $x$ that assures the delivery of intensity $I(x)$ at every point $x$ of the moving, deforming target [$I'(x)$ denotes a derivative of $I(x)$].

Provided the dose rate (intensity rate) of the accelerator is kept constant, and the condition (1) relating velocities $v_R$ and $v_L$ of a given pair of leaves of the MLC assembly is satisfied during irradiation for all instances $m$ and all points $x$ in the target, the desired intensity function $I(x)$ is delivered to the moving, deforming target. The relationship (1) indicates that pairs of leaf velocities for leading and following leaves have to belong to special $(m,x)$ parametrized, monotonically increasing curves (1) on plane $(v_R,v_L)$ in order to execute leaf motions that deliver the right intensity to deforming target. Thus, quite arbitrary choices of $v_R(m,x)$ allow one to match $v_L[m+I(x),x]$ so that (1) is true for all $m$ and $x$. The class of admissible solutions is reduced if the condition of containment of velocities of $v_R(m,x)$ and $v_L[m+I(x),x]$ to the square $S$, where $S=[(v_R(m,x),v_L[m+I(x),x])]: v_{\text{max}} \equiv v_R(m,x) \equiv v_{\text{max}}, v_{\text{max}} \equiv v_L[m+I(x),x] \equiv v_{\text{max}}$ (see Fig. 1) is imposed. This condition expresses the fact that speeds of leaves can not exceed in absolute terms the value of maximal velocity $v_{\text{max}}$ that design of MLC admits. Moreover, conditions of unidirectional motion of leaves in DMLC
The plot illustrates planar domains of the leading leaf speed $v_R$ and the following leaf speed $v_L$ as well as the mutual functional dependence of these leaf speeds at their passing over given point $x$ of the moving and deforming target. Restricted by MLC hardware limitations, the values of $v_R$ and $v_L$ are contained in the square bounded by lines $v_R = v_{max}$, $v_R = -v_{max}$, $v_L = -v_{max}$, and $v_L = v_{max}$. The condition of unidirectional motion of leaves (with respect to points of the target) constrains the above square to a parallelogram bounded by the lines $v_R = v_{max}$, $v_R = v_{max}$, $v_L = v_{max}$, and $v_L = v_{max}$. If over-restrictive condition (2) is additionally imposed, values for $v_R$ and $v_L$ are contained in the parallelogram $S_c$ bounded by lines $v_R = v_{max}$, $v_R = v_{max}$, $v_L = v_{max}$, and $v_L = v_{max}$. The monotonic curve $C$ represents the relationship (1) between $v_R[m + I(x)]$ and $v_L[m + I(x)]$, and displayed on the graph points $P_c$ define the optimal, for over-restrictive condition, evolution of leaves passing over given $x$ (at given $m$) for optimal and optimal-over-restrictive leaf evolutions, respectively.

For the purpose of deriving the algorithm for real-time DMLC IMRT delivery, we stress first that the relationship (1) is deduced assuming the target motion/deformation $y_f(m,x)$ is known a priori at any instant of time $m$ and for every target point $x$. This is not the assumption that can be carried to the real-time target motion registration situation, so formula (1) will have to be appropriately reinterpreted. However, before this is done it would be useful to define leaf evolutions that deliver the IMRT with over-restrictive conditions on leaf speeds.

The idea is that optimal trajectories of DMLC delivery with over-restrictive conditions provide a convenient reference solution for the real-time data leaf trajectories. The final calculations for real-time leaf trajectories can then be based on adjustments of a predetermined optimal-over-restrictive solutions. The over-restrictive bounds on leaf speeds should prevent violation, even when adjustments for real-time target motion perturbations are made, of leaf maximum velocities $v_{max}$.

Let us define the over-restrictive condition for leaf speeds by

$$v_R(m,x) \leq c \cdot v_{max}, \quad v_L(m + I(x),x) \leq c \cdot v_{max},$$

$$c \in [0,1],$$

(2)

that is to be satisfied for all points $x$ of the target and all moments $m$ over the interval of treatment delivery. Thus, the pair of velocities $(v_{R,off},v_{L,off})$ (superscripts $a,or$ in velocities $v_R$ and $v_L$ indicate that velocities $v_{R,off}$ and $v_{L,off}$ are derived for $a priori$ data setting with over-restrictive constraints) satisfying condition (2) have to be ultimately contained in the set

$$S_c = \{(v_R, v_L) : v_R \leq c \cdot v_{max}, v_L[m + I(x)] \leq v_{max} \}$$

(see Fig. 1). Formula (1) and constraint conditions $(v_R, v_L) \in S_c$ indicate that point $P_c$ with coordinates $(v_R = c \cdot v_{max}, v_L = v_{max})$ in Fig. 1 define the optimal, for over-restrictive condition, solution for evolution of leaves at each $x$ and $m$. Specifically, the point $P_c$ represents speeds of leading and following leaves at each $x$ and $m$ that after integration lead to optimal, for over-restrictive condition, evolution of leaves over all points $x$ of the target at all times $m$ (see Ref. 14). Formulas derived in Ref. 14 describe coordinates of points $P_c$ as given by

$$v_{R,off} = c \cdot v_{max}, v_{L,off} = v_{max},$$

$$m + I(x), x \}

(3)

[case (1)] or

$$v_{R,off} = \frac{c \cdot v_{max} - v_{L,off}^2[m + I(x),x]}{b^2 - (a^2)^{-1} \cdot I(x)} \cdot \left[ c \cdot v_{max} - v_{R,off}^2[m + I(x),x] \right] + v_{L,off}^2[m + I(x),x]$$

[case (2)]

Cases (1) and (2) above are defined by the curve on the $(v_R, v_L)$ plane intersecting vertical $[v_R = c \cdot v_{max};$ case (1)] or horizontal $[v_L = c \cdot v_{max};$ case (2)] boundary of the set $S_c$ (see Fig. 1), appropriately. Leaf trajectories for optimal delivery of intensity $I(x)$ for moving, deforming targets with velocity constraints conditioned as in (2) are therefore defined by equations 14.
\[
\frac{dv_{\text{L},\text{or}}}{dm} = \frac{c \cdot v_{\text{max}}}{b^2 - (d_L^2)' \cdot I'(x) \cdot \{c \cdot v_{\text{max}} - v_R^L(x, m + I(x))\}} + v_R^L(x, m) \quad \text{for case (1)}
\]

and

\[
\frac{dv_{\text{L},\text{or}}}{dm} = \frac{c \cdot v_{\text{max}}}{1 + (d_L^2)' \cdot I'(x) \cdot \{c \cdot v_{\text{max}} - v_R^L(x, m + I(x))\}} + v_R^L(x, m) \quad \text{for case (2)}
\]

Methods for solving systems of equations like (5) and (6) have been described in Refs. 12–14. How these solutions can be modified to reflect actual target motions registered in a real-time data setting [and still deliver the right intensity and not violate the constraint (2) with \(c = 1\)] will be shown in the next section.

**B. Solution for real-time data setting delivery based on optimal leaf trajectories for a priori target motion data setting with over-restrictive constraints**

When the \textit{a priori} data setting with over-restrictive conditions on leaf speeds is utilized for optimal control algorithms of DMLC IMRT for moving, deforming targets parameters \(b^4(m, x), d_R^4(m, x), v_R^4(m, x), \) and \(v_R^4[m + I(x), x]\) are determined in Eqs. (5) and (6) before solutions are calculated. They are treated as known (tabulated or analytically defined) functions of parameters \(x\) and \(m\) and allow one to determine leaf trajectories before delivery through integration of differential Eqs. (5) and (6). However, when the real-time approach is utilized values of parameters \(b^4(m, x), d_R^4(m, x), v_R^4(m, x), \) and \(v_R^4[m + I(x), x]\) are not predetermined for solutions of (5) and (6) to be implemented. As a result, the algorithm is not capable of determining leaf trajectories before delivery. The process of leaf trajectories definition has to be designed in this case through appropriate response to current reading of the motion of the target, i.e., it has to have an intrinsically local character—it can define the evolution of trajectories at any instance only through the infinitesimal step in time/space domain.

For real-time delivery of the predetermined intensity \(I(x)\) at any \(x\), the necessary local formula relating \(v_R\) and \(v_L\) that has to be satisfied uniformly over all \(x\) and \(m\) during the delivery is the relationship (1). However, in the real-time approach all parameters \(b(m, x), d_T(m, x), v_T(m, x), \) and \(v_T[m + I(x), x]\) of formula (1) are defined no earlier than at the moment they are registered. In particular, some of these parameters are defined after the speed \(v_R\) of the leading leaf has already been fixed. Thus, in this data setting formula (1) does not treat \(v_R\) and \(v_L\) equivalently. Choice of \(v_R\) at \((m, x)\) does not fix \(v_L\) at \([m + I(x), x]\) as parameters \(b\) and \(v_T\) at \([m + I(x), x]\) are not defined at \((m, x)\). On the other hand, at \([m + I(x), x]\), when the choice of \(v_L\) is made, \(v_R\) that has been fixed in the past, at \((m, x)\), is not adjustable. Thus, formula (1) under these circumstances is effectively used as a tool that allows matching uniquely \(v_L\) at \([m + I(x), x]\) to a predetermined \(v_R\) at \((m, x)\) [freedom of choice of values of \(v_R\) at \((m, x)\) makes it possible to satisfy \(v_R \leq v_{\text{max}}\). If so matched \(v_L\) at \([m + I(x), x]\) satisfies also the constraint condition limiting \(v_L\) leaf velocity to below \(v_{\text{max}}\), then both velocities \(v_R\) and \(v_L\) for leaf motions are physically admissible and they properly modulate the slope of intensity \(I(x)\) at \(x\) over moving/deforming targets.

Thus, the algorithm for leaf controls that leads to delivery of intensity \(I(x)\) over moving/deforming targets in real time is defined in the following steps (see Fig. 2):

\begin{enumerate}
  \item Points \(P = \{v_R^{a,ort}(m, x), v_L^{a,ort}[m + I(x), x]\}\) on plane \((v_R, v_L)\) that define optimized leaf trajectories for \textit{a priori} data setting with over-restrictive constraints are derived through formulas (3) and (4) for all \(x\)
\end{enumerate}

![Fig. 2. The plot illustrates functional dependence (1) between the leading leaf speed \(v_R\) (over-restricted) and the following leaf speed \(v_L\) (over-restricted) at the time of their passing over given point \(x\) of the moving and deforming target in the \textit{a priori} data setting (thin line) and modified functional dependence (7) between the leading leaf speed \(v_R\) (real time) and the following leaf speed \(v_L\) (real time) at the time of their passing over given point \(x\) of the moving and deforming target in the real-time data setting (thick line). Points \(P = \{v_R^{c,ort}, v_L^{c,ort}\}\) represent pairs of speeds of leading and following leaves passing over given \(x\) (at given \(m\)) for optimal-over-restrictive and real time leaf evolutions, respectively.](image)
and \( m \). See Fig. 1 and Fig. 2 where particular coordinates of point \( P_r \) are given by 
\[
\{v_R^{aR}(m,x), v_L^{aL}(m+I(x),x)\} = (c \cdot v_{\text{max}}, v_2).
\]

(ii) Registered in real-time motion of the target parameters \( v_R^{aR}(m,x) \) and \( v_L^{aL}(m,x) \) allow the adjustment of \( v_R^{aR}(m,x) \) to \( v_R^{aR}(m,x) \) (superscripts \( rt \) indicate that relevant quantities are derived in real-time data setting). The speed \( v_R^{aR}(m,x) \) of leading (right) leaf in real time at \( (m,x) \) is set so that the relative speed between leading leaf and the point \( x \) of the target is kept invariant from the \textit{a priori} to the real-time data setting. For application of this definition of \( v_R^{aR}(m,x) \), and its quantitative representation for calculated example, see formula (11) of the next section. In Fig. 2 the adjustment of the speed \( v_R^{aR}(m,x) = c \cdot v_{\text{max}} \) to \( v_R^{aR}(m,x) \) is represented by horizontal vector of length \( v_R^{aR}(m,x) - c \cdot v_{\text{max}} \).

(iii) Registered in real-time motion of the target provides parameters \( v_R^{aR}(m,x), v_L^{aL}(m+I(x),x), b^R(m,x), d^R(m,x), v_R^{aR}(m+I(x),x), v_L^{aL}(m+I(x),x) \), which are read into the following version of formula (1):
\[
v_L^{aL}(m+I(x),x) = \frac{b^R(m,x) \cdot [v_R^{aR}(m,x) - v_L^{aL}(m,x)]}{1 + (d^R)^2(m,x) \cdot I^R(x) \cdot [v_R^{aR}(m,x) - v_L^{aL}(m,x) \right] + v_L^{aL}(m+I(x),x).}
\]  
(7)

(iv) Values of the speed \( v_L^{aL}(m+I(x),x) \) of the following (left) leaf for all \( (m,x) \) are calculated from Eq. (7). In Fig. 2 the adjustment of the speed \( v_L^{aL}(m+I(x),x) \) to \( v_L^{aL}(m+I(x),x) \) is represented by vertical vector of length \( v_L^{aL}(m+I(x),x) - v_2 \).

(v) Pairs of leaf velocities \( \{v_R^{aR}(m,x), v_L^{aL}(m+I(x),x)\} \) defined in steps (ii) and (iv) determine the leaf trajectories \( v_R^{aR} \) and \( v_L^{aL} \) through successive increases of local leaf positions
\[
\Delta y_R^{aR}(m+\Delta m) = v_R^{aR}(m,x) \cdot \Delta m;
\]
\[
\Delta y_L^{aL}(m+I(x)+\Delta m) = v_L^{aL}(m+I(x),x) \cdot \Delta m,
\]  
(8)
with the change in the position \( \Delta x \) inside the target related to \( \Delta y_R^{aR} \) and \( \Delta y_L^{aL} \) through \( v_L^{aL}\).

Remark 1. Let us emphasize that the choice of constraint 
(2) that decides about the evolution of the trajectories in the \textit{a priori} data setting is quite arbitrary. For example, different values of the constant \( c \) in Eq. (2) can be utilized depending on the expected range of actual (real-time) velocities \( v_R^{aR}(m,x) \) of the target. In fact, the geometrical planar domain \( G \) restricting the pair of predefined velocities \( (v_R^{aR}, v_L^{aL}) \) may have more complex shape than the rectangular shape of set \( S_c \) (e.g., domain \( G \) may be specified as \( G = \{(v_R^{aR}, v_L^{aL}) : v_R^{aR} + v_L^{aL} = c \cdot v_{\text{max}}, c \in [0,1]\} \)). It is worth noting that any choice of the condition restricting mutual dependence of leaf speeds carries two risks. These risks can be illustrated in the simplest form when constraints specified by the set \( S_c \) are analyzed. One is that the following leaf actual speed \( v_L^{aL}(m+I(x),x) \), adjusted in real time, may exceed the maximum velocity constraint (this may happen if \( c \) is too close to 1). The second risk is related to extending excessively and unnecessarily the time of delivery (this may happen if \( c \) is too close to 0). The best one can do under these circumstances is to analyze statistically a large sequence of data on target motions, evaluate variability of target motions provided by these data, and chose parameter \( c \) (or, more generally, particular domain \( G \)) so that, at predetermined level of confidence, speeds \( v_R^{aR}(m,x) \) and \( v_L^{aL}(m+I(x),x) \) are contained in \( S_c \) (or \( G \)) over the time of actual treatment delivery.

Remark 2. In general, adjustments of speed \( v_R^{aR}(m,x) \) to \( v_R^{aR}(m,x) \) may not be necessary. The only true requirement to assure the proper delivery of the intensity over the target is that \( v_R^{aR}(m+I(x),x) \) in Eq. (7) is appropriately matched to velocity \( v_R^{aR}(m,x) \) [or to \( v_R^{aR}(m,x) \)] irrespective if one or the other is substituted in (7). However, from calculations performed for examples calculated in this paper we have found that solutions for leaf trajectories are more stable numerically if the speed \( v_R^{aR}(m,x) \) rather than \( v_R^{aR}(m,x) \) is utilized in Eq. (7).

C. Special cases of target evolutions

For the purpose of discussion of characteristic properties of real-time DMLC IMRT delivery, three specific classes of target motions can be distinguished.

(a) The first class of target motions admits arbitrary, though not reversing the order of target points, motions and deformations from the predefined target movements. These most general deformations are registered by imaging techniques in real time, and they provide continuously renewed functions \( b^R(m,x), d^R(m,x), v_R^{aR}(m,x), v_L^{aL}(m+I(x),x) \) in Eq. (7).

(b) Second class of target motions admits arbitrary changes in target translation motions but does not allow changes in target predefined deformations. Motions of the targets in this second class are consistent with the general inability of current registration algorithms to track changes of “inside target” points in real time. Thus, motions of targets characteristic of the second class can in general provide updated time and position functions \( v_R^{aR}(m,x) \) and \( v_L^{aL}(m+I(x),x) \) but they do preserve unchanged functions \( b^R(m,x), d^R(m,x) \) between \textit{a priori} and real-time data setting. Thus, for the second class of transformations Eq. (7) has the simplified form
\[
v_L^{aL}(m+I(x),x) = \frac{b^R(m,x) \cdot [v_R^{aR}(m,x) - v_L^{aL}(m,x)]}{1 + (d^R)^2(m,x) \cdot I^R(x) \cdot [v_R^{aR}(m,x) - v_L^{aL}(m,x) \right] + v_L^{aL}(m+I(x),x).}
\]  
(9)
Finally, the third class of target evolutions in the real-time data setting consists simply of rigid target motions (no target deformations in the a priori or in the real-time observed motion). For these, evolution functions expressing target deformations are identically equal to 1, i.e., \( b^R(m,x) = b^f(m,x) = 1 \) and \( d^R_f(m,x) = d^f_f(m,x) = 1 \), and Eq. (7) takes in this case the form

\[
v''_L[m + I(x), x] = \frac{v'_R(m, x) - v'_L(m, x)}{1 + I'(x) \cdot [v'_R(m, x) - v'_L(m, x)]} + v''_L[m + I(x), x]. \tag{10}
\]

For second and third classes of target evolutions in real time, the substitution (see step (ii) in the previous section)

\[
v''_R(m, x) = v''_R(a, m, x) + [v'_L(m, x) - v'_R(m, x)] \tag{11}
\]

for the speed \( v''_R(m, x) \) is equivalent to the formula

\[
v''_R(m, x) - v''_R(m, x) = v''_R(a, m, x) - v''_R(m, x), \tag{12}
\]

which has the following interpretation. If velocity of following leaf in real-time data setting \( v''_L[m + I(x), x] \) is compensated by local target velocity \( v''_R(m, x) \) (in real-time data setting), then \( v''_L[m + I(x), x] - v''_R(m, x) \) equals \( v''_R[a, m + I(x), x] \), i.e., to a priori velocity of the following leaf \( v''_R[m + I(x), x] \) compensated by local target velocity \( v''_R[a, m + I(x), x] \) (in a priori data setting). In other words, the formula

\[
v''_L[m + I(x), x] - v''_R[m + I(x), x] = v''_R[a, m + I(x), x] - v''_R[m + I(x), x], \tag{13}
\]

or

\[
v''_L[m + I(x), x] = v''_R[a, m + I(x), x] + [v''_R[m + I(x), x] - v''_R[m + I(x), x]], \tag{14}
\]

holds too. Formulas (11) and (14) show that, for the second (b) and the third (c) class of real-time target motions, a particularly simple solution exists. For the leading leaf the definition of velocity in real time at each \( (m, x) \) requires the addition of target motion perturbation \( [v''_L(m, x) - v''_R(m, x)] \) (registered in real time) to the a priori determined velocity solution \( v''_R(a, m, x) \). Similarly, the definition of speed of the following leaf in real time requires that at each \( (m + I(x), x) \) the target motion perturbation \( [v''_L[m + I(x), x] - v''_R[m + I(x), x]] \) (registered in real time) is added to the a priori determined velocity solution \( v''_L(a, m, x) \).

### III. RESULTS

To illustrate solutions for a real-time data setting, we present a sequence of examples. They span various intensity functions and various target motions. They show solutions in a real-time data setting, and for comparison they also show respective solutions for a priori data setting. Table I lists a full set of these examples and their relations to particular assumptions under which they have been calculated.

### A. Intensities

In the examples presented two intensity functions are delivered by DMLC IMRT. One intensity has the shape of double parabola and is expressed by the analytic formula

\[
I(x) = 2.133x^6 - 25.6x^5 + 111.59x^4 - 210.05x^3 + 148.28x^2 - 4.9641x.
\tag{15}
\]

The other intensity was originally extracted from a clinical IMRT plan. This intensity characterizes the IMRT optimized plan in the form of a one-dimensional histogram. Its approximated, smooth function representation can be described by a tenth-degree polynomial (see Fig. 3)

\[
I(x) = -0.5x^{10} + 11.83x^9 - 102.12x^8 + 91.02x^7 + 1449.2x^6 + 2704.5x^5 - 3163.7x^4 + 2213.0x^3 + 829.1x^2 + 125.5x + 5.
\tag{16}
\]

The domain of the function (16) extends over an interval of 4 cm in the case of a rigid target, and in the case of a deforming target the domain is variable and stretches from 2 to 8 cm with an equilibrium state extending over the distance of 4 cm.

### B. Target motions—a priori data setting for rigid targets

Rigid motions of the target will consist of purely oscillatory motions expressed by the analytic formula

\[
y_T(x, m) = A \cdot [1 - \cos(\omega_J \cdot m)], \quad \omega_J \gg 0,
\tag{17}
\]

where \( y_T(x, m) \in [0, y_T] \) for all \( m \) and for all \( x \in [0, x_T] \). Clinical motions are originally given in the form of one-dimensional time series and they are smoothed by interpolation procedures for actual calculations. Clinical (rigid target) motion characteristics can be read off from trajectories of target edges displayed in Fig. 4(a), Fig. 4(b), and Fig. 5.

### C. Target motions—a priori data setting for deforming targets

Deforming target motions are restricted in the examples calculated in this paper to “uniform deformations” by given by

\[
y_T(x, m) = \left(x - \frac{x_T}{2}\right) \cdot \left[\frac{1}{4} \cdot [5 + 3 \cdot \cos(\omega_k \cdot m)]\right] + A \cdot [5 - \cos(\omega_k \cdot m)].
\tag{18}
\]

Target deformations that are variable across the target, i.e., have local character, are not yet easily available from clinical data and so they will not be analyzed in our examples. In examples explicitly calculated in this paper the parameters \( A, x_T, \omega_J, \) and \( \omega_k \) have values given by \( A = 1 \text{ cm}, x_T = 4 \text{ cm}, \omega_J = 0.25 \text{ }1/MU \text{ and } \omega_k = 0.25 \text{ }1/MU \), except in the example displayed in Fig. 6(b), where \( \omega_J = 0.35 \text{ }1/MU \text{ and } \omega_k = 0.70 \text{ }1/MU \). Deforming target motion characteristics can be read off from trajectories of target edges displayed in Fig. 4(c), Fig. 6(b), and Fig. 7(b).
Table I. Listed below are solutions for leaf trajectories calculated for target motions that are known *a priori* and target motions that are provided in real time. Numerical calculations have been performed for two given intensities (double parabola intensity and clinically derived intensity) and for different patterns of target motions, both rigid motions and deforming (pulsating) motions of the target. For the *a priori* known target motions both optimal solutions (with maximum velocity constraints imposed) and suboptimal solutions (with over-restrictive velocity constraints imposed) are calculated. The real time solutions are derived from suboptimal solutions for leaf trajectories calculated for an *a priori* data setting. In all cases, the calculated number of monitor units for the total time of delivery is quoted for comparison. For cases when graphical representation of relevant leaf (and target) trajectories is provided, the number of the figure for a given example is quoted in the table.

<table>
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<tr>
<th></th>
<th><em>A priori</em> target motion data setting</th>
<th>Real time target motion data setting Random perturbation of target motion as in formula (19)</th>
<th>Deforming/pulsating target moving as in formula (18)</th>
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<td>Solid/rigid target moving as in formula (17) or derived from clinical observation</td>
<td>Solution based on real-time modification of trajectories for <em>a priori</em> target motion data setting obtained under over-restrictive constraint (2)</td>
<td>Deforming/pulsating target moving as in formula (18)</td>
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<td>Solid/rigid target moving as in formula (17) or derived from clinical observation</td>
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<td>Optimal solution time of delivery: 42.2 MU</td>
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<td>Modified solution time of delivery: 45.6 MU</td>
<td>Modified solution time of delivery: 43.6 MU</td>
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<td>Real-time delivery: 45.2 MU</td>
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<td>Leaf trajectories: Fig. 6(a)</td>
<td>Leaf trajectories: Fig. 6(b)</td>
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<td>Modified solution time of delivery: 25.9 MU</td>
<td>Modified solution time of delivery: 22.4 MU</td>
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<td>Real-time delivery: 26.9 MU</td>
<td>Real-time delivery: 22.1 MU</td>
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<td>Leaf trajectories: Fig. 4(a)</td>
<td>Leaf trajectories: Fig. 7(a)</td>
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<td>Leaf trajectories: Fig. 5</td>
<td>Leaf trajectories: Fig. 7(b)</td>
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<td>Real-time delivery: 27.2 MU</td>
<td>Real-time delivery: 22.1 MU</td>
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<td></td>
<td></td>
<td>Leaf trajectories: Fig. 8</td>
<td>Leaf trajectories: Fig. 7(b)</td>
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*A priori* target motion defined by analytic function.

Double parabola intensity (15).

Clinical intensity (16).

*A priori* target motion derived from clinical observation.

Clinical intensity (16).
D. Target motions—real-time data setting for rigid targets

These motions of target evolutions in real-time data setting are utilized in the examples depicted in Fig. 6(a), Fig. 7(a), and Fig. 8. They are defined by rigid target motions in the a priori data setting over which perturbations are imposed. Perturbations simulate the situation when in vivo motion data are being captured and transferred to leaf motion control algorithms at the time when leaves are moving over the target. The difference between the a priori and the real-time target velocities is that the real-time data are, in principle, unpredictable. Thus, to simulate these data in numerical calculations, they have to be input into algorithms as random processes. The simple yet realistic model of stochastic process \( \epsilon(m) \) defining random perturbations \( v_{i}^{*}(m,x) - v_{i}^{(a)}(m,x) \) of a priori defined target velocities \( v_{i}^{(a)}(m) \) can be described as a sum of independent random variables \( \Delta \epsilon(m_k) \) increasing over individual time intervals \( [m_k, m_{k+1}) \), \( k=1,2,\ldots,N \). Then, the cumulative effect \( \epsilon(m) \) is the sum of the random variables \( \Delta \epsilon(m_k) \) given as

\[
\epsilon(m) = \sum_{i=k}^{i=x} \Delta \epsilon(m_i); \quad m \in [m_k, m_{k+1});
\]

where \( r_i \) and \( R_i \) are random variables uniformly distributed over the interval \([0, 1]\) and \( \alpha \) and \( \beta \) are two fixed constants from the interval \([0, 1]\). Notice that constant \( \alpha \) has the interpretation of the size of the velocity perturbation and \( \beta \) determines the likelihood of the perturbation of the velocity taking place over the given interval \([m_k, m_{k+1})\). In our examples of real-time deliveries depicted in Fig. 6(a), Fig. 7(a), and Fig. 8, lengths of intervals \([m_k, m_{k+1})\) have been set to 0.01 MU and constants \( \alpha \) and \( \beta \) have been set to \( \alpha = 0.02 \) cm/MU and \( \beta = 0.8 \), appropriately.

E. Target motions—real-time data setting for deforming targets

These motions of target evolutions in the real-time data setting are utilized in examples depicted in Fig. 6(b) and Fig. 7(b). They are defined by deforming target motions in the a priori data setting over which spatially uniform, time-dependent random perturbations are imposed. These perturbations are given by formula (19).

F. Summary of leaf trajectories properties

For all examples calculated in Table I, for which over-restrictive conditions on maximal leaf speeds are imposed, the assumed constraints are given by formula (2) with parameter \( c \) equal to 0.7.

It is worthwhile to pay attention to the following characteristic features of the leaf trajectories for DMLC IMRT delivery in the a priori and the real-time data setting that have been calculated in the examples charted in Table I,

(i) For all solutions the intended intensity function, being it analytic double parabola (15) or clinically derived fluctuating intensity function (16), is delivered as originally planned.

(ii) For all solutions, those defined in the a priori data setting as well as those defined in the real-time data setting, the constraint on maximum admissible speed of leaves of 1 cm/MU is at all times satisfied.

(iii) Among solutions for leaf trajectories obtained in the a priori data setting and constrained by maximum admissible speed of leaf velocities (1.0 cm/MU), the (optimal) solution minimizing the time of delivery exists. For solutions in the a priori data setting that admit overconstrained conditions for the maximum admissible speed for leaf velocities, the optimality of the DMLC IMRT delivery is achieved with respect to new constraints of 0.7 cm/MU. However, these solutions are suboptimal relative to solutions obtained under constraint of true maximal speeds of leaves (1.0 cm/MU).

(iv) As discussed in the Introduction, the solutions, in real-time data setting, deliver the proper intensity and satisfy the conditions imposed by limitations of the maximum admissible speed (1 cm/MU) for leaves in the laboratory frame of reference. However, MLC leaves in the real-time delivery do not, at each moment, travel with the maximum speed admissible and thus do not deliver irradiation to the target in the minimal time achievable (this minimal time can be calculated only a posteriori).

IV. DISCUSSION

When computing trajectories of leading and following leaves, we updated in our examples target data velocities at every discrete step on the time axis in which parameters of trajectories were calculated in our programs (i.e., every 0.01
MU/H20850. As a result of instantaneous updates, the calculated real-time delivery of intensity is not quantitatively different from the intensity that was intended to be delivered. In clinical applications, instantaneous update of target data velocities is not possible and thus the error in modulated intensity delivery associated with delay in reading target data motion will be introduced. To minimize this error one can envision adaptive filtering techniques predicting future motion of the target from current and past data should be applied for real-time delivery.

All approaches to real-time tracking with DMLC require that one measure the target positions and speeds on the time scale comparable with the time scale of transmission of leaf control data itself (approximately 50 ms). In radiation therapy.

**FIG. 4.** The figure displays three plots of trajectories of leading (thick solid line) \( y_R \) and following (gray solid line) \( y_L \) leaves that deliver the clinical intensity (16) of Fig. 3 in the \( a \) \( priori \) data setting. (a) The target oscillates as the rigid rod along the y axis [see formula (17)] and its motion is represented by dashed lines that correspond to motions of right and left edges of the one-dimensional (rod-like) target. Maximum admissible speed of leaves is set to 1 cm/MU. Optimal trajectories \( y_R \) and \( y_L \) are functions of time \( m \) (expressed in MU). It is worth noting that, due to the nonzero value of intensity at both edges of the target, the trajectory \( y_L \) of optimal following (left) leaf moves with the left edge of the target for 5.0 MU from the moment of treatment commencement. Similarly, at the conclusion of irradiation the trajectory \( y_R \) of the leading (right) leaf reaches the right edge of the target at 19.6 MU and moves in coincidence with this edge of the target till the following leaf reaches the right edge of the target at 24.6 MU, i.e., at the moment of termination of the irradiation. (b) The graph illustrates leaf trajectories for the case identical to the one illustrated in (a) with the difference that over-restrictive constraint on leaf speeds is imposed with \( c=0.7 \) (i.e., maximum admissible speed of leaves is set to 0.7 cm/MU). (c) Trajectories of leading (thick solid line) \( y_R \) and following (gray solid line) \( y_L \) leaves deliver the clinically derived intensity (16) of Fig. 3 to oscillatory, uniformly deforming target (motion/deformation defined by formula (18) with \( A=1 \) cm, \( x_F =4 \) cm, \( \omega_0=0.25 1/MU \), \( \omega_g=0.25 1/MU \)). The maximum admissible speed of leaves is set to 0.7 cm/MU (\( c=0.7 \)). Dashed lines correspond to motions of right and left edges of the one-dimensional, deforming target and star-dotted lines correspond to motions of points \( x=1 \), \( x=2 \), and \( x=3 \) of the target.
The preferred method to locate the target site is via radiography. This may be done by (1) imaging the tumor itself; (2) imaging anatomical structures that are rigidly connected to the tumor; (3) detecting radiographically artificial fiducial markers that are implanted in or near the tumor; and (4) tracking through imaging better visible, surrogate organs that move in synchrony with the tumor. The choice of method depends on the nature of the motion and the location and visibility of the tumor.\cite{1,11,16,20} Most comprehensive information on three-dimensional target positioning and deformation in real time can be found by registering the targeting radiograph through the computed tomography (CT) study used for treatment planning. This can be done by matching the radiographs to digitally reconstructed radiographs calculated from the CT data.\cite{1,2}

However, image registration based exclusively on anatomic features is computationally intensive, making it difficult to acquire new target positions in the time scale required for DMLC real-time delivery. In addition, only occasionally, can the tumor be discerned with sufficient precision in radiographs. Therefore, the most appropriate approach to image registration for soft tissue is through tracking fiducial markers implanted in the tumor. In this case, the tumor position, orientation, and deformation can be found by registering changes in its outline defined by the treatment planning CT using the fiducial markers. As in most instances, the tumor itself cannot be seen well enough in the tracking radiograph to segment and register so the surrogate landmarks must be used. Fiducial-based guidance has the advantage that the fiducial markers are comparatively easy to locate with automatic image processing tools, and the position determination involves only a simple algebraic calculation. Thus, the time needed to make a position determination can be on the order of 50 ms, enabling real-time fluoroscopic tracking of the markers.\cite{3,16,17} The disadvantage is the invasiveness of the

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**Fig. 5.** The thick, solid line illustrates trajectory $y_R$ of leading leaf and the gray, solid line illustrates trajectory $y_L$ of the following leaf that delivers clinically derived intensity (16) to a 4 cm wide rigid target whose motion is derived from clinical observations. Irregular, fluctuating motion of the target is depicted by dashed lines that represent motions of right and left edges of the one-dimensional, rod-like target that initially occupy coordinates $y_{\text{edge}}(0)=7.1$ cm and $y_{\text{edge}}(0)=11.1$ cm. The maximum admissible speed of leaves is set to 0.7 cm/MU ($c=0.7$). Trajectories $y_R$ and $y_L$ are functions of time $m$ (expressed in MU). The calculations are performed in the a priori target data setting. Due to a nonzero value of intensity at both edges of the target, the trajectory $y_L$ of the following leaf moves in coincidence with the left edge of the target at 21.9 MU and moves in coincidence with this edge of the target until the following leaf reaches the right edge of the target at 26.9 MU at the moment of termination of the irradiation.

**Fig. 6.** The figure displays two plots of trajectories of leading (thick, solid line) $y_R$ and following (gray, solid line) $y_L$ leaves that deliver double-parabolic intensity (15) in the real-time data setting. (a) Leaf trajectories are solved first for a priori defined rigid target motion (17) and over-restrictive speed constraint [condition (2) with $c=0.7$] and modified appropriately for real-time target motion perturbations. Target motions in real time are defined through addition of random perturbations (19) over the predefined target motions (17). Irregular, randomly perturbed motion of the target is depicted by dashed lines that represent motions of right and left edges of the one-dimensional rod-like rigid target of width of 4 cm. (b) Displayed leaf trajectories are found by the modification of optimal leaf trajectories solved for a priori defined target deforming motion (18) and over-restrictive speed constraint [condition (2) with $c=0.7$]. Deformation of the target is illustrated by displaying trajectories of five points of the target: two edges of the target (target x coordinates $x=0$ and $x=4$ and laboratory system coordinates $y=0$ and $y=8$ at $m=0$) and three internal points defined by $x=1$, $x=2$, and $x=3$ with laboratory system coordinates $y=2$, $y=4$ and $y=6$ at $m=0$. 

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likely be necessary.\textsuperscript{21-23} Adaptive filters are commonly used in real-time control processes that must synchronize a response to input signals produced by mechanisms that are unknown or noisy. Adaptive filtering is based on the empirical characteristics of the signal itself. In its simplest form, a predictive filter collects samples of a signal for a period of time and makes a best estimate of the next discrete sample of the signal from a weighted linear combination of the past samples. If the signal is stationary the filter will rapidly converge to an optimal estimate of the signal at a future point in time.

The errors in intensity delivery may also be caused by constraints on leaf acceleration (which are not taken into account in our considerations). As maximal values for leaf accelerations are truly large (\(>50\text{ cm/s}^2\)) we do not expect that these constraints will introduce noteworthy inaccuracies in intensity delivery. Nevertheless, it would be beneficial in future investigations to calculate quantitatively errors in delivery caused by not accounting for acceleration constraints. Moreover, the errors in intensity delivery may be caused by excessive speeds of the target that may occur at delivery (coughing, etc.). If increased target speeds are not exceeding maximum admissible \(v_{\text{max}}\) speeds of leaves, then regulating the dose rate (MU/s) of the accelerator would increase appropriately the maximum allowable speed of leaves (in cm/MU). This in turn would allow one to adjust the speed of leaves (in cm/MU) necessary for delivery of proper intensity profile. If, however, increased target speeds do exceed the maximum admissible speeds of the leaves, then the beam hold would provide the only solution capable of delivering the planned dose without error. In these cases the correlation procedure. This approach to target tracking in real time makes therefore most probable utilization of DMLC IGRT delivery in real time that was derived in this paper.

To decrease errors, caused by the delay of image data transfer in real-time delivery to DMLC control algorithms, adaptive filter techniques compensating for these delays will...
of leaf and target motions will have to be preserved to allow the resumption of treatment without distortion of the beam intensity profile over the moving target.

Finally, let us observe that the real-time IMRT delivery to moving target described in this work deals strictly with target motions parallel to the leaf motion. If there exists a target motion component perpendicular to the leaf motion, the formalism presented here needs to be extended to avoid artifacts associated with this target motion component. In all likelihood these more general models would require synchronization of MLC leaf pair motions (in the a priori as well as in the real-time data setting approaches) along the lines discussed in Ref. 24.

V. CONCLUSION

The results of this paper demonstrate that the real-time DMLC delivery of IG IMRT with multileaf collimators is achievable if image data for the target motions are provided in real time to the MLC controls. The method of solution presented in this work is based on earlier developed models of DMLC motions delivering IMRT treatments to moving rigid and deforming targets.21–24 These earlier models relied on solutions of differential equations that were identified through predetermined data of target motions. The basic postulate of earlier models was that a priori target motion data are available in advance, and they define trajectories of leaves to be executed at treatment. However, when data on target motions are collected at time of delivery the defining of MLC leaf motions is not possible through globally determined, over all space and time variables, differential equations. Nevertheless, if relations between velocities of leading and following leaf motions are enforced following real-time input of target motion data, the DMLC IMRT treatment in real time is still properly executed. The key is to constantly modify leaf velocities, following the acquisition of the real-time target motion data, so that matching of leading and following leaf velocities is achieved which guarantees proper shaping of intensity slope above each target point. In consequence, the real-time adaptation of local speeds of leaves as defined in this paper leads to properly accumulated delivery of modulated intensity over the whole target. The ability to adapt leaf motions to a given pattern of intensity without violating limitations on maximum leaf speeds, and without interruption of treatment continuous delivery, can be assured only statistically, with presumed level of confidence.

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