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Motion Compensation for Robotic Lung Tumour Radiotherapy in Remote Locations: a Personalised Medicine Approach

Clara M. Ionescu*, Cosmin Copot and Dirk Verellen

Abstract—The purpose of this work is to integrate the concept of patient-in-the-closed-loop application with tumour treatment of cancer-diagnosed patients in remote areas. The generic closed loop control objective is effective synchronisation of the radiation focus to the movement of a lung tissue tumour during actual breathing of the patient. This is facilitated by accurate repositioning of a robotic arm manipulator, i.e. we emulate the Cyberknife Robotic Radiosurgery system. Predictive control with disturbance filter is used in this application in a minimalistic model design. Performance of the control structure is validated by means of simulation using real recorded breathing patterns from patients measured in 3D space. Latency in communication protocol is taken into account, given telerobotics involve autonomous operation of a robot interacting with a human being in different location. Our results suggest that the proposed closed loop control structure has practical potential to individualise the treatment and improves accuracy by at least 15%.

Index Terms—cyberknife robotic radiosurgery system, model based predictive control, real-time tumour tracking, stereotactic body radiosurgery, telerobotics

I. INTRODUCTION

NOWADAYS, radiation therapy is a major modality for treating cancer patients. Stereotactic Body Radiotherapy (SBRT) is an overarching term addressing cancer treating radiotherapies that exploit the principle of hypo-fractionation with high precision tumour localization and image guidance [1]–[7]. This technique sequences a high radiation dose over multiple non-coplanar beams that only intersect at the cancerous target location, thereby creating a so called localised radiation hot-spot. Tumours nestled in lung tissue or near thoracic organs are often found to describe a spatial trajectory as a result of respiration induced lung movement [9]. The phenomenon is referred to as *respiratory (induced) tumour motion* and the spatial path described by the tumour as the *tumour trajectory*. Hence, precise target localisation and accurate dose delivery cannot be guaranteed if this complex motion is not taken into account.

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Respiratory gated radiotherapy (RGR) represents a static perspective on motion-adaptive therapy. The technique exploits the periodic nature of the breathing cycle and administers a cyclic radiation exposure. Therefore the radiation source can remain fixed in space and is only switched on when the target moves into a predefined window or gate. Position and width of this gate depend on the specific behaviour of the target movement, the current angle of incidence and consequently the exposed adjacent healthy tissue [7], [10].

Real-time tumour tracking (RTTT) is a recent addition to the SBRT family, that caters to the respiratory induced tumour movement [7], [11]–[14]. The technique entails active compensatory motion to counteract any wandering of the tumour, such that the relative position between radiation beam and target is kept constant. This motion compensation can be realized either by manipulating the collimating system, the entire linac or using the patient support system [10]. In the Cyberknife approach the source is mounted on a six degree of freedom robotic arm to facilitate sufficient manoeuvrability. Individual beams are directed precisely to the target while the patient is exposed to the radiation [8].

In practice, surrogate breathing signals that exhibit strong correlation to the actual tumour trajectory are measured, and fed to a *correlation function* which then estimates the true tumour position. Surrogate signals can be obtained by use of implanted fiducial markers, however this requires an invasive procedure [15], [16]. Alternatively, surrogate signals can be provided by external markers such as infrared reflectors interwoven into a vest worn by the patient during treatment [17]. Recently, a new technique arose that completely circumvents any direct contact to the patient. Continuous-wave (CW) radar sensors measures the periodic motion of the body itself thereby minimizing the discomfort experienced by the patient. The technique however is yet in its infancy but shows great potential in motion-adaptive radiotherapy [18].

Using any of these surrogate techniques will heavily influence the quality of the estimates given by the correlation functions. These consist of patient specific mathematical algorithms apriori designed based on the surrogate signals and tumour trajectory signals obtained through conventional imaging. As the surrogate signals are correlated to an accurate estimate of the tumour trajectory and these motion patterns change during treatment, the accuracy of the correlation model needs to be verified. This verification is performed online by comparison of intermediate tumour images and their positional estimates [4], [19]. Whenever accuracy would fall short,

Fig. 1. Conceptual scheme of various elements of remote robotic radiotherapy system.

treatment is interrupted and the function revised, which is to be avoided as much as possible in clinical practice.

In the context of telemedicine, virtual presence of a medical supervisor and remote delivery of treatment have a significant role in today's healthcare. Telemedicine has several advantages, the main being economic cost effective, and in restricted access situations (i.e. space) it may play a unique role. In today's framework of cyber-physical systems, long distance teleoperations are common control problems. Some of the main challenges for control are: latency, nonlinear dynamics and constraints. For instance, the communication delays may vary from 0.08 s to as much as 600 s depending on the distance from Earth communication base to various places in Space [20]. A schematic overview of the remote robotic radiotherapy system is given in figure 1. The potential for biomedical applications of telemedicine in remote areas has already been recognized [21], [22] and suggestions for surgical robotic support in space missions has been proposed in [23]. Furthermore, procedures to circumvent any potential faults for space robotic systems have been proposed in [24]. An important challenge remains the presence of time delays, which may deteriorate significantly the performance if not suitably tackled [25].

The original contribution of this paper stands in the following. Firstly, we introduce and tailor the use of closed loop control algorithms for motion compensation in robotic radiotherapy. Inverse kinematics of the robotic motion are used to partially compensate dynamic motion profiles during radiotherapy and simplify the closed loop control complexity, but dynamic models of the robotic system are also used in the control algorithm. Secondly, we employ the use of 3D patient-breathing profiles into a model based predictive control methodology to ensure a patient-specific motion compensation. The above described steps aim at moving away from the current state of art in clinical practice, which uses solely robot inverse kinematics and open loop compensation based on motion sensor systems. Additionally, we employ the proposed predictive control scheme in a Smith Predictor form,

such that it can naturally deal with varying time delays. The use of breathing profiles as disturbance profiles introduces a feedforward-like action in dynamic motion compensation. The purpose of the entire methodology is to increase accuracy in the position of the robotic radiotherapy system to maintain to a minimum the percent of healthy tissue radiation.

The paper is organized as follows: next section introduces the robot kinematics and our specific approach to this problem. Section 3 presents the proposed control methodology followed by results and discussion in section 4. A conclusion section summarizes the main outcome of this work.

II. ROBOT MODELS

A simplified representation of the robotic manipulator that is employed in the Cyberknife Robotic Radiosurgery system is given in figure 2.

Fig. 2. Visualisation of the coordinate frames fixed to each link body on the Cyberknife robot.

A *serial-link manipulator* consists of a chain of links interconnected with a set of joints, each DOF, either rotational or translational. A robot consisting of n joints, numbered from 1 to n , comprises $n + 1$ links, 0 and $n + 1$ respectively corresponding to the robot base and the end-effector [12], [26]. The full state of a robot can thus be captured by a generalised joint variable vector $\bar{q}(t) = [q_1(t) \dots q_n(t)]^T$ containing the joint variables. Notice that a seventh coordinate frame is attached to the radiation focus point in figure 2.

Each transformation matrix consist of a rotation matrix ${}^{i-1}R_i$ and a translation vector ${}^{i-1}T_i$. Assembling into one transformation matrix ${}^{i-1}DH_i$ and concatenating frame $i - 1$ to frame i gives:

$${}^{i-1}DH_i = \begin{bmatrix} {}^{i-1}R_i & {}^{i-1}T_i \\ 0 & 1 \end{bmatrix} \quad (1)$$

This formulation obeys the transition law presented in equation (2), which demonstrates its ease of use when describing the transformation between consecutive coordinate frames:

$${}^jG_i = {}^jG_{i-1} {}^{i-1}DH_i \quad (2)$$

whereas the matrix nDH_R specifies the position of the beam that is to be synchronised to the tumour, with respect to the mounting plate and the following relation is used:

$$\begin{aligned} {}^0G_R(\bar{q}) &= {}^0DH_1(q_1) \dots {}^{n-1}DH_n(q_n) {}^nDH_R \\ &= \begin{bmatrix} {}^0E_R(\bar{q}) & {}^0P_R(\bar{q}) \\ \bar{0} & 1 \end{bmatrix} \\ &= \mathcal{K}(\bar{q}) \end{aligned} \quad (3)$$

where three degrees of freedom are found in the end-effector position 0P_R as well as in the rotation matrix 0E_R , therefore exhibiting a six dimensional nature.

Since the objective of this study is to accurately synchronise the radiation focus with the tumour trajectory, we determine the end-effector state containing the orientation and position of the radiation source and therefore the radiation focus. From the perspective of the treatment we obtain a reference end-effector state and the number of DOF that should be addressed by the reduced inverse kinematic solution. Some considerations are listed below, while taking into account current possibilities.

- As the XYZ trajectories described by the tumour do not extent to a large volume, the reference end-effector state can be adjusted to the trajectory center and the desired reference angle of incidence.
- The mathematical description of the orientation of the ray and hence the angle of incidence coincides with the base vectors of the coordinate frame fixed to the end-effector. From the treatment perspective it is not required to maintain a precise angle of incidence, i.e. the corresponding DOF can be eliminated.
- The position of the radiation focus is described by the position of the end-effector. Since the objective is to synchronise the tumour trajectory and the radiation focus, it is necessary to address the corresponding DOF in the reduced inverse kinematics.

Consequently, we reduce the problem to the DOF in the position vector P_R . The reference end-effector state G_R^{ref} is used to cover the averaged angle of incidence and averaged tumour position. Perturbations, caused by the respiratory-induced motion, are counteracted by varying the two last joints. The perturbation caused with respect to the desired G_R , δG_R , will by definition adapt the following form:

$$\delta G_R = \begin{bmatrix} \delta E_R & \bar{0} \\ \bar{0} & 0 \end{bmatrix} \quad (4)$$

The reduced inverse problem is visualised in figure 3. The dimensions used to emulate the real-life Cyberknife are given by the following matrices for the reduced models:

$${}^4R_5 = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos(q_5) & -\sin(q_5) \\ 0 & \sin(q_5) & \cos(q_5) \end{bmatrix}, {}^4T_5 = \begin{bmatrix} 0 \\ 0.215 \text{ m} \\ 0 \end{bmatrix} \quad (5)$$

$${}^5R_6 = \begin{bmatrix} \cos(q_6) & 0 & \sin(q_6) \\ 0 & 1 & 0 \\ -\sin(q_6) & 0 & \cos(q_6) \end{bmatrix}, {}^5T_6 = \begin{bmatrix} 0 \\ 0.215 \text{ m} \\ 0 \end{bmatrix} \quad (6)$$

$${}^6R_R = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}, {}^6T_R = \begin{bmatrix} 0 \\ 0.25 \text{ m} \\ -1.25 \text{ m} \end{bmatrix} \quad (7)$$

Fig. 3. Geometrical visualisation of the reduced inverse kinematics problem with respect to 0G_4 .

The desired coordinates, x_T , y_T and z_T , are first transformed to the fourth coordinate frame, recall figure 2. As the first four joints are fixed, this coordinate frame is constant, as well as the corresponding transformation matrix. Classical inverse kinematics are then used to obtain a static feedforward compensation of robotic arm position.

Each robot joint is equipped with a high accuracy lower-level closed-loop joint control unit. The closed loop joint dynamics can modelled as second order transfer functions with unit gain and joint specific damping ratio ζ_i , and frequency ω_i :

$$P_i(s) = \frac{\omega_i^2}{s^2 + 2\zeta_i\omega_i s + \omega_i^2} \text{ with } i \in \bar{q} \quad (8)$$

The specific joint parameters are enlisted as follows: for the fifth joint we have that $\omega_5 = 3\pi$; $\zeta_5 = 0.9$, and for the sixth joint $\omega_6 = 4\pi$; $\zeta_6 = 1$, respectively. These parameters have been selected such that to mimic as close as possible the real dynamic profile of the radiotherapy Cyberknife robot available on location at TROP in Brussels. The transfer functions in continuous and discrete-time are given below:

$$P_5(s) = \frac{3\pi}{s^2 + 5.4\pi s + 9\pi^2} \quad (9)$$

$$P_5(q^{-1}) = \frac{0.1823q^{-1} + 0.1156q^{-2}}{1 - 0.9587q^{-1} + 0.2566q^{-2}} \quad (10)$$

$$P_6(s) = \frac{4\pi}{s^2 + 8\pi s + 16\pi^2} \quad (11)$$

$$P_6(q^{-1}) = \frac{0.267q^{-1} + 0.1361q^{-2}}{1 - 0.7302q^{-1} + 0.1333q^{-2}} \quad (12)$$

and are a fairly good dynamic response approximations.

Since we are working with digital signals, a sampling period of 80 ms is used. This value ensures reliable numerical discretization of the robot dynamics as well as the breathing pattern of the patient. The discretized versions of the the transfer functions given above were used as the polynomial models for control design, while the continuous transfer functions were used as the real processes and were implemented in the Simulink program for the purpose of simulation.

III. PREDICTIVE CONTROL METHODOLOGY

The closed loop control structure proposed hereafter operates at a higher hierarchic level supervisory to the lower-level

robot joint control units and has the task of generating the lower-level joint reference signals for the local controllers. For the purpose of feedback information, the tumour positions are available at every time instant t using sensing techniques [18].

A. General model prediction output

Since the breathing of a person is periodic in nature and represents a disturbance signal for tracking accurately the position of the tumour, a natural closed loop control solution is predictive control. This is a class of control strategies making use of a process model and of a disturbance model. We propose here to employ our own algorithm, i.e. the extended prediction self-adaptive control (EPSAC). This algorithm has been introduced first in the early 80s [27] and updated in its nonlinear form later on [28]. The method proved very successful in other robotic applications [29]. Briefly, EPSAC uses the process model defined as in:

$$y(t) = x(t, u) + n(t) \quad (13)$$

with $y(t)$: (measured) process output; $u(t)$: process input; $x(t)$: model output; $n(t)$: (calculated) process disturbance and $e(t)$: uncorrelated (white) noise. The disturbance $n(t)$ includes the effects in the measured output $y(t)$ which are not resulting from the input $u(t)$ applied to the process model. Both the process model $x(t) = \frac{A(q^{-1})}{B(q^{-1})} \cdot u(t)$ as well as the noise model $n(t) = \frac{C(q^{-1})}{D(q^{-1})} \cdot e(t)$ are interpreted as linear filters and represented by monic polynomials in the backwards shift operator [28]. The strategy makes use of a prediction horizon N_2 , a control horizon N_u and a delay vector N_1 .

The fundamental step in EPSAC consists in the prediction of the future process output values $y(t+k|t)$ at time instant t over a prediction horizon N_2 indicated by the parameter k , based on:

- the measurements available at time instant t :

$$\begin{bmatrix} y(t) & y(t-1) & \cdots & u(t-1) & u(t-2) & \cdots \end{bmatrix}$$
- the postulated future values:

$$\begin{bmatrix} u(t|t) & u(t+1|t) & \cdots & u(t+N_2|t) \end{bmatrix}$$

Using the generic process model from equation (13), the forecasting step becomes:

$$y(t+k|t) = x(t+k|t) + n(t+k|t) \quad (14)$$

in which $x(t+k|t)$ and $n(t+k|t)$ are computed by use of filtering techniques on the process- and noise model [28].

The future response is treated as the cumulative result of two components:

$$y(t+k|t) = y_{base}(t+k|t) + y_{optimize}(t+k|t) \quad (15)$$

with:

$$y_{base}(t+k|t)$$

- effect of past control

$$\begin{bmatrix} u(t-1) & u(t-2) & \cdots \end{bmatrix}$$
- effect of a *base* future control scenario, called $u_{base}(t+k|t)$, $k \geq 0$, which is defined a priori. For linear systems however the choice is irrelevant, making the simple choice $u_{base}(t+k|t) \equiv 0$ appropriate

- effect of future (predicted) disturbances $n(t+k|t)$

$$y_{optimize}(t+k|t)$$

- effect of the *optimizing* future control actions

$$\begin{bmatrix} \delta u(t|t) & \delta u(t+1|t) & \cdots & \delta u(t+N_u-1|t) \end{bmatrix}$$

 with $\delta u(t+k|t) = u(t+k|t) - u_{base}(t+k|t)$
 and N_u a design parameter.

The component $y_{optimize}(t+k|t)$ is interpreted as the cumulative result of a series of *impulse* inputs and a *step* input.

As such the effect of impulse with amplitude $\delta u(t+l|t)$ occurring at time instant $t+l$ is compromised in a contribution $h_{k-l}\delta u(t+l|t)$ to the process output at time instant $t+k$. A final step input $\delta u(t+N_u-1|t)$ at time $t+N_u-1$ results in a contribution $g_{k-N_u+1}\delta u(t+N_u-1|t)$ to the predicted process output at time instant $t+k$. The coefficients $h_1, h_2, \dots, h_{N_2}$ and $g_1, g_2, \dots, g_{N_2}$, respectively the impulse- and steps response of the system, are calculated from the process model. In case of linear systems, they can be calculated only once, and apply the superposition principle. The cumulative effect is given by:

$$y_{optimize}(t+k|t) = h_k\delta u(t|t) + h_{k-1}\delta u(t|t) + \cdots + g_{k-N_u+1}\delta u(t+N_u-1|t) \quad (16)$$

Using the matrix notation, relations (15) and (16) can be summarised in the following key equation:

$$\mathbf{Y} = \bar{\mathbf{Y}} + \mathbf{G}\mathbf{U} \quad (17)$$

with

$$\begin{aligned} \mathbf{Y} &= [y(t+N_1) \quad \cdots \quad y(t+N_2)]^T \\ \bar{\mathbf{Y}} &= [y_{base}(t+N_1|t) \quad \cdots \quad y_{base}(t+N_2|t)]^T \\ \mathbf{U} &= [\delta u(t|t) \quad \cdots \quad \delta u(t+N_u-1|t)]^T \\ \mathbf{G} &= \begin{bmatrix} h_{N_1} & h_{N_1-1} & \cdots & g_{N_1-N_u+1} \\ h_{N_1+1} & h_{N_1} & & g_{N_1-N_u+2} \\ \vdots & & \ddots & \vdots \\ h_{N_2} & h_{N_2-1} & \cdots & g_{N_2-N_u+1} \end{bmatrix} \end{aligned}$$

A mathematical cost function $\mathcal{V}$, minimized over $\mathbf{U}$ is used:

$$\mathcal{V}(\mathbf{U}) = \sum_{k=N_1}^{N_2} (r(t+k|t) - y(t+k|t))^2 \quad (18)$$

with N_1 and N_2 , being design parameters for delay and prediction horizons, respectively. This cost function is of quadratic form and using the matrix notation of equation (17):

$$\mathcal{V}(\mathbf{U}) = [\mathbf{R} - \bar{\mathbf{Y}} - \mathbf{G}\mathbf{U}]^T [\mathbf{R} - \bar{\mathbf{Y}} - \mathbf{G}\mathbf{U}] \quad (19)$$

with R the reference trajectory. For the unconstrained linear case, the optimal solution is given by [27], [28]:

$$\mathbf{U}^* = [\mathbf{G}^T \mathbf{G}]^{-1} \mathbf{G}^T (\mathbf{R} - \bar{\mathbf{Y}}) \quad (20)$$

The actual control input $u(t)$ can thus be computed and applied to the process:

$$u(t) = u_{base}(t) + \mathbf{U}^*(1) \quad (21)$$

The net advantage of this formulation is that numerical complexity is minimal without loss of performance.

B. Including information on periodic disturbance

The disturbance model $C(q^{-1})/D(q^{-1})$ usually contains an integrator, to ensure zero steady state error. However, since the signal $n(t)$ can be calculated from equation (13), its PDS (power density spectrum) can be applied online to extract the main frequency component f_0 when periodic disturbances are present. This knowledge can be incorporated in the disturbance filter design by addition of poles close to the unity circle around the main frequency f_0 [30]:

$$\frac{1}{(1 - q^{-1})(1 - ae^{j\alpha}q^{-1})(1 - ae^{-j\alpha}q^{-1})} \quad (22)$$

where the parameter $\alpha = 2\pi f_0 T_s$ is a discretized expression of the filter frequency, f_0 , with T_s the sampling period. The parameter $a \leq 1$ is a design lever governing the proximity of the poles to the unity circle and therefore the accuracy of the model, hence the amplitude given by the parameter a is directly related to the distinctiveness of the peak at frequency f_0 in the frequency response and therefore tightly interwoven with the accuracy of the forecast. If the disturbance frequency is well known, a value ≈ 1 is recommendable. However, if the disturbance frequency is subject to some uncertainty a value between 0.8-0.9 is advised [30], [31].

In the context of this application, two main sources of disturbances are present: movement of the patient and movement of the tumour during breathing. The first source, patient movement, is directly tackled by the standard integrator in the loop. This affects the tumour position as well, tackled in its periodicity stemming from breathing pattern by the optimized design of the disturbance filter as described above.

C. Dealing with variable time-delays

As observed in figure 1, variable latency can be expected in communication. For a system with time delay, changes in the controlled variable are noticeable once the time delay has passed. Therefore, in order to find the optimal control sequence only output predictions occurring after the time delay should be taken in the cost function. This means that the minimum costing horizon N_1 should be equal to the time delay. Then the maximum prediction horizon N_2 can be set to an appropriate value that ensures a stable and robust response and the control loop can be operated with fixed controller parameters.

For a variable time delay however, the value of N_1 (and thus also N_2) varies with the dead-time index. This implies a continuously varying matrix size and computational complexity may increase significantly from one sampling instant to the next. We propose therefore a control structure as illustrated in figure 4.

Figure 4 depicts the Smith-Predictor like EPSAC formulation for processes with variable time delays [32]. At each sampling instant, the delay-free model output $x(t)$, resulting from the process dynamics only, is calculated using the stored values $[x(t-1), \dots, u(t-1), \dots]$. At the same sampling instant, the variable time delay is estimated/computed. Once the delay value in samples N_d is known, $x(t - N_d)$ can be selected out of the stored x -values, such that the delayed model output $z(t) = x(t - N_d)$.

Fig. 4. Smith-Predictor like EPSAC formulation for processes with different time delays or variable time delays.

In this way, the prediction procedure is thoroughly simplified, resulting in a Smith predictor-like scheme, with separation of the tank and tube dynamics on one hand and the varying time delay on the other hand. In such approach the minimum prediction horizon is no longer varying and obviously equal to one. Hence, the maximum prediction horizon is also constant.

D. Stability Issues

The following assumptions in the MPC control algorithm apply:

- the predictions are made over input-output models and the disturbance filter
- the control and prediction horizon are not equal
- there are no terminal constraints
- there is no terminal cost
- there is no terminal control law

The finite horizon constrained optimal control problem in the input-output formulation in equation (19) translates to the following minimization problem in state-space:

$$\min_U \sum_{k=N_1}^{N_2} (r(t+k|t) - x(t+k|t))^2 + \lambda \cdot \sum_{k=0}^{N_u-1} u(t+k|t)^2 \quad (23)$$

subject to $\Delta u(t+k|t) = 0, \forall k \in [N_u, N_2]$ with $\Delta u = u(t+k|t) - u(t+k-1|t)$, $x(t+k|t) \in \wp \forall k \in [N_1, N_2]$ and λ a weighting factor of the control effort. The proof is given in [33] and this equivalence allows one to map all definitions and constraints from input-output based model formulation to state space and discuss stability without terminal constraints.

Definition: the i -step robust controllable set $\tilde{K}_i$ is the set of states in $\wp$ which can be driven by an admissible input sequence of length i to an arbitrary target set T in exactly i steps, while guaranteeing the evolution of the states inside $\wp$ for the $i-1$ steps for all disturbances:

$$\begin{aligned} \tilde{K}_i &= x(t) \in \mathbb{R}^n | \exists u(t+k|t) \in U_0^{i-1} \\ x(t+k|t) &\in \wp |_{k=1}^{i-1} \in \wp \\ x(t+i|t) &\in T, \forall n(t+k|t) |_{k=1}^{i-1} \end{aligned} \quad (24)$$

Definition: an i-step robust tunnel set $\tilde{L}(\wp)$ is an i-step robust admissible set $\tilde{C}_i(\wp)$ subject to the constraint that the admissible control sequence remains constant:

$$\tilde{L}_i = \tilde{C}_i(\wp) | \delta u(t+k) = 0 \quad (25)$$

Definition: the robust feasible set $\tilde{X}_F$ is the set of states for which an admissible control sequence exists that satisfies the state/output constraints for all disturbance sequences.

Theorem: the robust feasible set $\tilde{X}_F(\wp, N_u, N_2)$ is given by

$$\tilde{X}_F(\wp, N_u, N_2) = \tilde{K} | N_u(\wp, \tilde{L} | N_2 - N_u)(\wp) \quad (26)$$

where $\tilde{L}$ is a robust tunnel set, $\wp$ is the admissible states set, $\tilde{K}$ is the robust controllable set.

Proof: the construction of the robust feasible set can be divided into two parts in time by approaching it from the end. In the horizon given by $N_2 - N_u$ the requirement is to keep the control moves constant to an admissible set $\tilde{K}$ which satisfy the constraints set $\wp$, for all disturbances. This represents the robust tunnel set given by $\tilde{L} | N_2 - N_u)(\wp)$. The requirement over the control horizon N_u is to find the control sequence that satisfies the state constraints and lies in the target set $\tilde{L} | N_2 - N_u)(\wp)$. This is given by the robust controllable set $\tilde{K} | N_u(\wp, \tilde{L} | N_2 - N_u)(\wp)$ which is an overall robust feasible set.

The closed loop MPC-EPSAC operation within the robust tunnel set is considered as safe for the performance objectives. Any deviation from this set can be considered to generate an error warning to the operator. The proposed algorithm is such tailored to meet the patient specificity as given hereafter. A fault detection algorithm has not been taken within the purpose of the current study.

IV. PROPOSED PATIENT-SPECIFIC CONTROL METHODOLOGY

For the application of closed loop control with individualised patient information we make use of i) robot related and ii) tumour related signals. The robot related signals are:

- $P_R(t) = [x_R(t) \ y_R(t) \ z_R(t)]^T$: Radiation focus or end-effector position, expressed in Euclidean coordinates.
- $q_R(t) = [q_5(t) \ q_6(t)]^T$: Radiation focus or end-effector position, expressed in the robot joint variable space.
- $\hat{q}_R(t) = [\hat{q}_5(t) \ \hat{q}_6(t)]^T$: Reference signals for the lower level robot joint control.

And the tumour related signals are:

- $P_T(t) = [x_T(t) \ y_T(t) \ z_T(t)]^T$: Tumour position, expressed in Euclidean coordinates. This signal is the result of the online tumour tracking system and is known up to time t .
- $q_T(t) = [q_{5,T}(t) \ q_{6,T}(t)]^T$: Tumour position, expressed in the robot joint variable space. Computed through application of the reduced inverse kinematics on $P_T(t)$.

The control objective being the accurate synchronisation of $P_R(t)$ to $P_T(t)$, or expressed equivalently in the robot joint variable space, $q_R(t)$ to $q_T(t)$. Hence, the supervisory control algorithm provides the appropriate reference signals, $\hat{q}_R(t)$, to the robot lower-level control.

We choose the following base vectors to which the control variable is related:

$$\Delta_i(t) = q_{i,R}(t) - q_{i,T}(t) \Rightarrow \Delta(t) = [\Delta_5(t) \ \Delta_6(t)]^T \quad (27)$$

Consequently, one obtains a new reference trajectory vector:

$$\hat{\Delta}_i(t) = q_{i,T}(t) - q_{i,T}(t) \equiv 0 \Rightarrow \hat{\Delta}(t) = [\hat{\Delta}_5(t) \ \hat{\Delta}_6(t)]^T \quad (28)$$

The complete process model, including the filtering sequences resulting in the tumour position coordinates P_T and the subsequent application of reduced inverse kinematics, is given in figure 5, with the following filter designs for each coordinate signal:

$$\frac{1}{(1 - q^{-1})(1 - a_i e^{j\alpha_i} q^{-1})(1 - a_i e^{-j\alpha_i} q^{-1})}, \quad i \in \{x, y, z\}$$

and the lower level closed loop joint dynamics:

$$\frac{A_j(q^{-1})}{B_j(q^{-1})} = \frac{\omega_j^2}{s^2 + 2\zeta_j \omega_j s + \omega_j^2}, \quad j \in \{q_5, q_6\}$$

Fig. 5. Schematic representation of the EPSAC formulation for robot and tumour position model prediction.

The complete control structure is illustrated in figure 6. The proposed algorithm can be summarized as follows:

- compute the tumour position $P_T(t)$, by detection of the surrogate breathing signals fed to the correlation model, encapsulated in the *detector* block.
- forecast of the tumour position by the *prediction model* block, which includes the disturbance model.
- translate the future tumour trajectory $q_T(t+k|t)$ in robot coordinates by application of the reduced inverse kinematics on the tumour position forecast, as well as a computation of the future robot joint values $q_R(t+k|t)$ based on the postulated input vector $\hat{q}_R(t+k|t)$ and robot model (14).
- determine the control vector $\Delta(t)$ by subtraction upon optimizing the current model input $\hat{q}_R(t)$ (27).

V. RESULTS AND DISCUSSION

A simulation study was performed to illustrate the efficiency of the proposed approach. Since the tumour position is available from real patients undergoing lung tumour radiotherapy, we have injected these signals in the system as disturbances

Fig. 6. Full size feedback loop. The EPSAC prediction steps are explicitly displayed to emphasize the control structure.

occurring from the desired position of the radiation beam. Once the system is initialised with positions for all flexible joints, the measured signals in closed loop may be used to extract online the information upon the disturbance frequency f_0 . The disturbance filter in EPSAC given in (22) is then adapted online. A preliminary simulation analysis with a fixed information was employed to detect the optimal prediction horizon value, while maintaining the control horizon $N_u = 1$ sample and varied delay between 0.4 (5 samples) - 60 (750 samples) seconds. The initial disturbance filter design was for $f_0 = 0.2783$ Hz and amplitude $a = 0.75$. The prediction horizon was chosen $N_2 = 3$ samples, as a result of an optimization procedure leading to the lowest RMS values, as depicted in figure 7 for control variable Δ_5 . Similar results are obtained for the control variable Δ_6 . Supervisory control was applied on the two last robot joints. The latency is introduced between feedback signals and processing unit in a remote location. This illustrates the overall principle given in figure 1.

Fig. 7. Performance curves for various tuning of the prediction horizon for control variable Δ_5 .

Initiation of the simulator for the robot joint location was given as:

$$\bar{q}^{ref} = \left[\frac{\pi}{4}; \frac{\pi}{8}; \frac{\pi}{8}; \frac{\pi}{8}; -\frac{\pi}{4}; 0 \right]$$

The breathing patterns characterising in 3D the tumour trajectory have been provided by TROP in Brussels and are given in figure 8. They indicate the relative tumour position coordinates with respect to the tumour trajectory center. Notice

that the amplitude in the y direction is about three times as large as the amplitude in x and z direction.

Fig. 8. Relative tumour trajectory with respect to the trajectory center.

The result of the closed loop control is given in figure 9 for the joint vector $q_R = [q_{5,R} \ q_{6,R}]^T$, the tumour position expressed in the robot joint variable space, $q_T = [q_{5,T} \ q_{6,T}]^T$, and the actual control variable vector $\Delta = [\Delta_5 \ \Delta_6]^T$, with the latter shifted to the corresponding reference joint value for clarity. The result indicates that the controller has successfully synchronized the radiation focus and tumour position. Figure 10 depicts the corresponding lower-level reference signals $\hat{q}_5$ and $\hat{q}_6$ to the local joint controllers. Given the predictive nature of the control, a positive phase shift is present in the reference signals. Hence, the control undertakes action before the actual disturbances occur, thereby successfully circumventing the manifestation of lag between the radiation focus and the tumour position.

Figure 11 depicts the corresponding radiation depth which is constrained to 1 cm. This depends heavily on the length of the radiation beam possibly the depth will be less in real life applications.

Fig. 9. Output variables. Simulation results of the synchronisation of the radiation focus to the real time tumour position.

Fig. 10. Control effort. Simulation results of the synchronisation of the radiation focus to the real time tumour position.

Two other 3D tumour position from two other patients were also tested in simulation and the results are summarized in

Fig. 11. Radiation depth variation.

TABLE I
OVERVIEW OF RMS FOR ALL TESTED DATA

Data	RMS open loop	RMS closed loop	added accuracy %
Patient #1	898	747	16.8%
Patient #2	1136	985	13.3%
Patient #3	912	781	14.4%

table I as a function of the total RMS error between the actual position and desired position. The results indicate that a significant improvement in accuracy is achieved by introducing the proposed closed loop feedback compensation algorithm.

VI. LIMITATIONS OF THIS STUDY

Any work has a set of limitations when perspectives are foreseen. In this section we mention those most proximal to the next steps which can be executed to further improve the proposed methodology and augment its performance.

The effect of other possible disturbances, such as patient movement, is not explicitly taken into account. However, the disturbance filter in EPSAC includes an integrator, which corrects for deviations other than those stemming from the periodic breathing of the patient. Other disturbances such as coughing will affect the position of the tumour as well, for a fraction of the time leading to radiating possible healthy tissue. Such abrupt changes in the tumour location may be rejected in closed loop only, given the bandwidth of the controller/actuators is large enough. This is also part of the mechanical design of the radiotherapy robot and an embedded control design must be performed hand-in-hand of the two components.

Error-recovery routines have not been addressed here, assuming the patient is lying steady on the pre-defined position and that no sensor/actuator failure occurs. Of course, reality is more complex, and a fully worked out assist device platform has not been executed. Indeed, a manifold of other issue await to be addressed, e.g. rate limitations, hard nonlinearities, fault tolerant control, etc. Possibly auto-tuning of control algorithm to unforeseen conditions may be necessary, as suggested in [34].

There is also an important degree of nonlinearity involved when tumour dynamics are considered in 3D. In this paper we tackle everything from a linear system point of view, while tumour shapes, size and movement during breathing is a complex nonlinear variable. The nonlinear EPSAC algorithm has been presented in [28]. In essence, is an iterative version of the linear EPSAC, hence does not require a significant increase in numerical complexity. Convergence is achieved by minimizing the error in the $y_{optimize}$ term from equation (16). For this purpose, tumour models are necessary, some of which are available in the literature [35]–[37].

VII. CONCLUSIONS

This paper introduces the benefits of closed loop control for improving accuracy in the position control of a robot arm during radiotherapy of lung tumour tissue. The proposed scheme tackles active disturbance (effects of breathing) and variable latency intervals. The successful combination of predictive control, disturbance filter design and Smith predictor scheme allow improvement in accuracy of 15%. Personalised model based control medicine is therefore enabled for remote areas.

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