

Autonomous Drugs Optimal Management, Part II: Liver Tumor Impedance Control in Radiofrequency Ablation using I-first order and I-P Compensators Compared with a PID Controller

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Abstract:

This paper is the second in a series of research papers studying the autonomous drug optimal management. It handles the control of the liver-tumor impedance associated with radiofrequency ablation using an I-first order and an I-P compensators from the second generation of control compensators. Some tuning techniques for the proposed compensators are proposed based on zero/pole cancellation and using the MATLAB optimization toolbox. The step time response of the control system using the proposed compensators is presented and compared with that of a conventional PID controller from the first generation of PID controllers tuned in a previous research work. The comparison reveals the best controller/compensator among the three ones presented depending on a graphical and quantitative comparison study for reference input tracking.

Keywords — Liver tumor impedance control, I-first order compensator, I-P compensator, PID controller, controller/compensators tuning.

I. INTRODUCTION

Radiofrequency ablation (RFA) is a localized image guided treatment using thermal energy to remove or destroy tumor tissue without damaging the surrounding tissue [1]. However, when applying the RFA to liver tumor patients a serious problem emerges which is the ‘roll-off phenomenon’ which is a sudden increase in the tumor tissue impedance under certain conditions. The roll-off results in losing power supply to the electrode of the FRA apparatus and longer treatment time [2], [3]. The solution of this problem is to control the supply voltage of the apparatus to eliminate the roll-off completely through automatic control [4]. We start by presenting a literature review about this important subject since 2000:

Grasso et al. (2000) outlined that thermally-mediated interstitial systems able to induce tissue necrosis by means of heat produced by waves frequency emitted from a generator and delivered through electrode into the liver tumor. They stated that the RFA system uses a wave frequency in the range of 480-500 kHz. They presented scientific reports about the application of RFA to treat liver cancer in patients of numbers between 12 and 48 and tumor size between 10-60 mm [5]. Medical Advisory Secretariat (2004) presented a review of the evidence on the safety, clinical effectiveness and cost-effectiveness of RFA compared with other treatments for unresectable hepatocellular (HCC) in Ontario. They outlined that high frequency alternating electrical currents applied to the tumor tissues to kill the tumor. They concluded that the

RFA is safe, (perhaps) more effective than the percutaneous ethanol injected to treat HCC and more cost effective than the injected percutaneous ethanol [6]. Hinshaw et al. (2006) evaluated the clinical efficacy of the intraperitoneal installation of 5% dextrose in water during RFA of peripheral liver tumors for decreasing the post-RF pain. They outlined that patients subjected to this technique reported significant less pain in the first 24 hours after the procedure. They concluded that pretreatment with intraperitoneal solution before RF decreased pain and time of hospital stay [7]. Garvais et al. (2009) outlined that the choice of liver ablation as well as between percutaneous and surgical approaches depended on tumor factors, patient factors and viable treatment options. Besides, they stated that the results of RFA varied mainly with tumor size [8].

Minami and Kudo (2011) presented an overview for the current status of RFA for HCC to make this technique applicable in clinical practice. They reviewed the technical development of the RFA probe design and provided a profile of side effects and information on the integration of RFA into patients with HCC [9]. Zhang et al. (2013) outlined that thermal ablation is increasingly being used for liver tumors with RFA having effective tumor ablation and less time consumption. They presented the state of the art of the RFA technique including theoretical development, experimental study, clinical application and future issues [10].

Hof et al. (2018) analyzed short-term and long-term outcomes of RFA in simultaneous treatment of primary tumor and liver metastases. They concluded that RFA should be considered as a useful alternative to liver resection (removal of a liver part by surgical procedure) [11]. Sato et al. (2020) outlined that the RFA has been accepted as a minimally invasive therapeutic treatment for liver malignancies applied for small tumors (< 3 cm) and large liver tumors. They reviewed the recent refinement of liver RFA and provided technical tips [12]. Salah et al. (2022) outlined that the RFA is one of emerging therapeutic modalities used for the minimally invasive treatment in the management of early-stage of HCC. Their study results revealed that two-thirds of patients had an unsatisfactory

level of knowledge about HCC and RFA. They recommended health education programs for HCC patients using new teaching methods (such as home videos and computer-assisted instructions) [13].

Faria et al. (2024) investigated the efficiency of a bioinspired particle swarm optimization approach to PID controller tuning in RFA for liver tumors. Based on ex-vivo experiments, they identified a 9th order continuous-time transfer function model for the tumor impedance. Through PID controller they achieved a step time response with 0.605 % maximum overshoot and 2.87 s settling time. They concluded that using a tuned PID controller offered a practical solution to enhance RFA effectiveness contributing to the advancement of the RFA technique [14]. Maruyama et al. (2025) outlined that RFA is less invasive and provides faster postoperative recovery compared to surgery. They presented the role of ultrasound in ablation for liver cancer and its specific usage [15]. Yang et al. (2025) compared the prognosis between liver resection and RFA in patients with solitary HCC ≤ 3 cm. They concluded liver resection provided better measures than RFA for patients with solitary small HCC (≤ 3 cm) [16].

II. THE CONTROLLED TUMOR IMPEDANCE AS A PROCESS

- Faria et al [14] run clinical test on liver tumor patients and investigated the occurrence of the roll-off phenomenon accompanying the application of the radiofrequency ablation (RFA) technique. They identified a 9th order transfer function model $G_p(s)$ for the tumor impedance given as [14]:

$$G_p(s) = N(s)/D(s) \quad (1)$$

Where:

$$N(s) = 32.43s^8 + 135s^7 + 510.3s^6 + 925.7s^5 + 1104s^4 + 829.7s^3 + 556.9s^2 + 58.83s + 0.81 \quad (2)$$

$$D(s) = s^9 + 2.12s^8 + 15.76s^7 + 21.61s^6 + 55.2s^5 + 46.8s^4 + 49.14s^3 + 24.45s^2 + 7.28s + 0.50 \quad (3)$$

- The unit step time response of the tumor impedance process defined by Eq.1 with $N(s)$ and $D(s)$ given by Eqs.2 and 3 is shown in

Fig.1 as generated by the step command of MATLAB [17] for a 30 V RFA input.

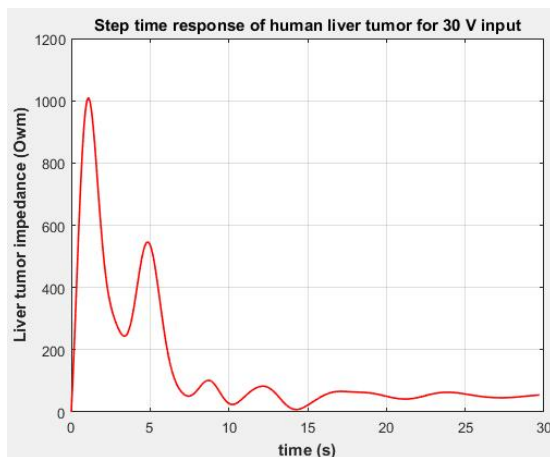


Fig.1 Step time response of the tumor impedance as a process.

COMMENTS:

- Maximum overshoot: 1977.6 %
- Settling time to ± 2 % tolerance: 15.236 s
- Rise time: 0.0365 s
- Maximum impedance: 1000 Ω

III. CONTROLLING THE LIVER TUMOR IMPEDANCE USING A PID CONTROLLER

- The conventional PID controller is one of the controllers of the first generation of PID controllers. It is still in use in some engineering and medical applications such as liver tumor treatment [14], drug scheduling for cancer treatment [18] and torque control of tumor growth models [19]. A PID controller has a transfer function, $G_{PID}(s)$ given by:

$$G_{PID}(s) = K_{pc1} + (K_{i1}/s) + K_{d1}s \quad (4)$$

- The PID controller has three gain parameters: proportional gain K_{pc1} , integral gain K_{i1} and a derivative gain K_{d1} tuned for good performance for the control system.
- Faria et al [14] tuned the PID controller for the tumor impedance of Eq.1 using the particle swarm optimization technique and provided the following tuned controller parameters:

$$K_{pc1} = 5.0594; K_{i1} = 10; K_{d1} = 0.4959 \quad (5)$$

- With the PID controller tuned, Eq.5 is used to plot the step time response of the liver tumor impedance control system using the MATLAB 'step' and 'plot' commands [17] providing the step time response shown in Fig.2 for a desired liver tumor impedance of 180 Ω .

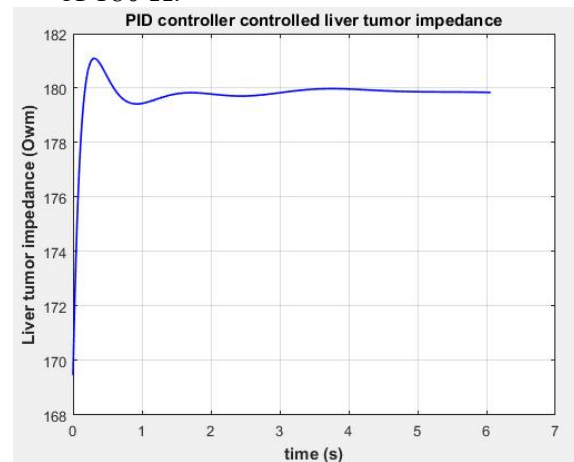


Fig.2 Step time response of a PID controlled liver tumor impedance.

COMMENTS:

- Maximum overshoot: 0.605 %
- Settling time to ± 2 % tolerance: 2.870 s
- Rise time: 0.127 s
- Steady-state error: zero

IV. CONTROLLING THE LIVER TUMOR IMPEDANCE USING AN I-FIRST ORDER COMPENSATOR

- The I-first-order compensator is one of the second generation of control compensators introduced by Prof. Galal Hassaan since 2014. The I-first order compensator was proposed to control serum hemoglobin level [20], serum low density cholesterol [21], serum oxygen [22], serum pH [23], blood urine nitrate (BUN) [24], serum pCO₂ [25], serum phosphate concentration [26], serum magnesium concentration [27] and serum potassium concentration [28]. It has the transfer function $G_{c2}(s)$ given by [20]:

$$G_{c2}(s) = (K_{c2}/s)[(s+z_2)/(s+p_2)] \quad (6)$$

Where:

K_{c2} = compensator gain

z_2 = compensator zero

p_2 = compensator pole

- The I-first-order compensator is set in a single-loop control system block diagram just before the process and after the error detector receiving the error signal as an input.
- The three parameters of the I-first-order compensator are tuned as follows:
 - ✚ The tumor impedance transfer function in Eq.1 has a simple pole at -0.0932 ($s+0.932$).
 - ✚ The zero/pole cancellation technique [29] is applied to the open-loop transfer function of the block diagram loop for the tumor impedance control. The compensator zero (in Eq.6) is chosen to cancel the simple pole ($s+0.0932$) of the tumor impedance process providing the value of the compensator zero as:

$$z_2 = 0.0932 \quad (7)$$

- ✚ The transfer function of the closed-loop control system, $M_2(s)$ is deduced using Eqs.1 and 6 in a unit feedback single loop control system.
- ✚ Now, we have two parameters of the I-first order compensator (K_{c2} and p_2) to be tuned for good performance of the control system for the tumor impedance.
- ✚ An ISTSE performance index [30] is used to optimize the two compensator parameters using the MATLAB optimization toolbox [31].
- ✚ The tuned compensator parameters using this proposed technique are given by:

$$K_{c2} = 0.014799, p_2 = 0.012918 \quad (8)$$

- The step time response for reference input tracking of 180Ω desired tumor impedance using the compensator transfer function in Eq.6 and process transfer function in Eq.1 is obtained using the command 'step' of MATLAB [17] as shown in Fig.3.

COMMENTS:

- Maximum overshoot: zero
- Settling time to $\pm 2\%$ tolerance: 39.290 s
- Rise time: 20.963 s
- Steady-state error: zero

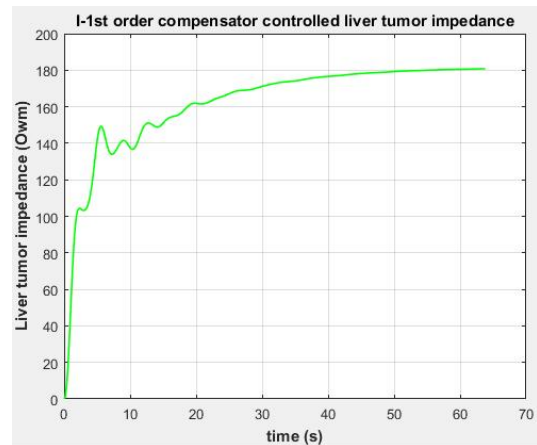


Fig.3 Step time response of an I-first order compensator-controlled liver tumor impedance.

V. CONTROLLING THE LIVER TUMOR IMPEDANCE USING AN I-P COMPENSATOR

- The I-P compensator is a novel compensator design belonging to the second generation of control compensators introduced by prof. Galal Hassaan (one of the authors) since 2014. An I-P compensator consists of two control elements: An I-control mode, $G_{I3}(s)$ in the forward path just after the error detector and before the controlled process and a P-control mode, $G_{P3}(s)$ in the feedback path of the single-loop control system proposed to control the liver tumor impedance process. It has the transfer function equations:

$$G_{I3}(s) = K_{i3}/s, G_{P3}(s) = K_{pc3} \quad (9)$$

Where:

K_{i3} = compensator integral gain

K_{pc3} = compensator proportional gain

- The two parameters of the I-P compensator are tuned as follows:
 - ✚ The transfer function of the closed-loop control system for the control of the tumor impedance of the liver using an I-P compensator is derived and used to find the ISTSE performance index [30] which is then minimized using the MATLAB optimization toolbox [31].
 - ✚ The result of the tuning operation reveals the following two gain parameters of the I-P compensator:

$$K_{i3} = 55.255, K_{pc3} = 1.0 \quad (10)$$

- The step time response for reference input tracking of 180Ω desired tumor impedance using the compensator transfer function in Eq.9 and process transfer function in Eq.1 is obtained using the command 'step' of MATLAB [17] as shown in Fig.4.

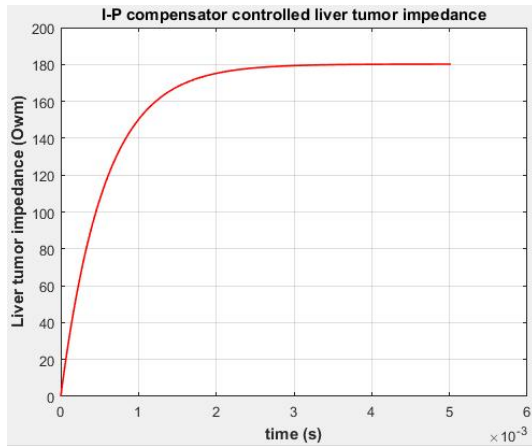


Fig.4 Step time response of an I-P compensator-controlled liver tumor impedance.

COMMENTS:

- Maximum overshoot: zero
- Settling time to $\pm 2\%$ tolerance: 0.0450 s
- Rise time: 0.0012 s
- Steady-state error: zero

VI. COMPARISON ANALYSIS

- To evaluate the effectiveness of using the proposed compensators, the step time response for a desired liver tumor impedance of 180Ω is compared with that using a PID controller tuned in reference [14].
- A graphical comparison is presented in Fig.5 showing three step time responses for I-first order, I-P compensators and PID controller.
- A quantitative comparison for the time-based characteristics of the control systems proposed to control the human liver tumor impedance is given in Table 1 for reference step input tracking (desired impedance).

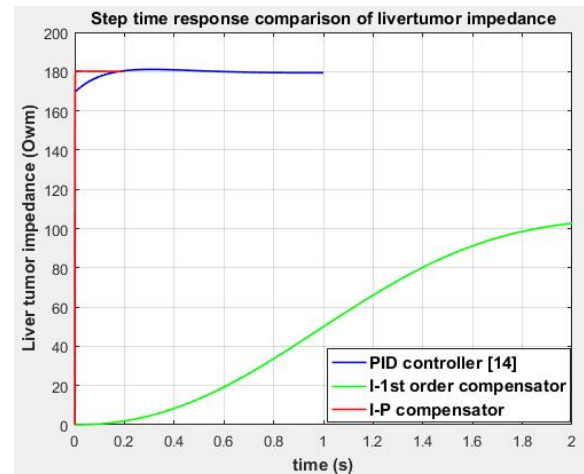


Fig.5 Liver impedance control using one controller and two compensators.

TABLE 1
CHARACTERISTICS COMPARISON FOR LIVER-TUMOR IMPEDANCE CONTROL

Characteristics	Without control	PID controller	I-first-order compensator	I-P compensator
$OS_{\max} (\%)$	1977.6	0605	0	0
$T_{s2\%} (s)$	15.836	2.871	39.29	0.0019
$T_r (s)$	0.0365	0.127	20.963	0.0012
$e_{ss} (\Omega)$		0	0	0

$OS_{\max}$ = maximum percentage overshoot

$T_{s2\%}$ = settling time to 2 % tolerance.

T_r = rise time.

e_{ss} = steady-state error.

VII. CONCLUSIONS

- This research paper investigated the use of I-first order and I-P compensators from the second generation of control compensators compared with a PID controller from the first generation of PID controllers to control the impedance of the liver-tumor to help in avoiding the cut-off phenomena during the radiofrequency ablation applied to some liver-cancer patients.
- The process under control was identified in a previous research work by a 9th order transfer function model producing a step time response having 1977.6 % maximum overshoot. This complex process is an example of complex processes representing real channel for control engineer to control and produce good performance.
- The performance of the proposed compensators was assigned through the investigation of the step time response of the

control system comprising the compensator and the liver-tumor impedance process.

- The tuning technique used to optimize the compensators parameters was based on the zero/pole cancellation technique and using the optimization toolbox of MATLAB and an ISTSE performance index.
- The two proposed compensators succeeded to eliminate completely the maximum percentage overshoot of the closed-loop control system for reference input tracking compared with 0.605 % for the PID controller.
- The settling time of the step input tracking time response (for 2 % tolerance) was assigned to be 39.29 and 0.0019 s for the I-first order and I-P compensators compared with 2.871 s for the PID controller.
- The proposed compensators succeeded to provide a step time response having a rise time of 20.963 and 0.0012 s for the I-first order and I-P compensators compared with 0.127 s for the PID controller.
- The proposed compensators and the PID controller succeeded to provide step time response for reference input tracking without any steady-state error.
- The I-P compensator has proved in this application to be the best controller/compensator because of its outstanding step time response without any overshoot, undershoot or steady-state error with settling time less than 2 ms.
- Therefore, the I-P compensator was selected in this research work as the best controller/compensator to control the liver-tumor impedance for roll-off free radiofrequency ablation.

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DEDICATION



Al-Biruni statue in Tahrir

MOHAMMED IBN AHMED AL-BIRUNI [32]

- He was born in Birun of Iran in 973 AC.
- He was pioneer in mathematics, astronomy, pharmacy, engineering and philosophy.
- He wrote about 148 books and treatises.
- One of his books was the ‘*Pharmacy in Medicine*’.
- He defined the qualifications of a ‘*pharmacist*’ and the definition of pharmacy as a science.
- He presented a classification for ‘*learning pharmacology*’ in three stages: preliminary stage, advanced stage and final stage (practice).
- This is why we dedicate our research work in this research paper to the great scientist Al-Biruni.