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The design of a robotic multichannel platform for photodynamic therapy

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Abstract

A compact robotic platform is designed for simultaneous multichannel motion control for light delivery and dosimetry during interstitial photodynamic therapy (PDT). Movements of light sources and isotropic detectors are controlled by individual motors along different catheters for interstitial PDT. The robotic multichannel platform adds feedback control of positioning for up to 16 channels compared to the existing dual-motor system, which did not have positioning encoders. A 16-channel servo motion controller and micro DC motors, each with high resolution optical encoder, are adopted to control the motions of up to 16 channels independently. Each channel has a resolution of 0.1mm and a speed of 5cm/s. The robotic platform can perform light delivery and dosimetry independently, allowing arbitrary positioning of light sources and detectors in each catheter. Up to 16 compact translational channels can be combined according to different operational scheme with real-time optimal motion planning. The characteristic of high speed and coordinating motion will make it possible to use short linear sources (e.g., 1- cm) to deliver uniform PDT treatment to a bulk tumor within reasonable time by source stepping optimization of multiple sources simultaneously. Advanced robotic control algorithm handles the various unexpected circumstance in clinical procedure, e.g., positiontorque/current control will be applied to prevent excessive force in the case of resistance in the fiber or motorized mechanism. The robotic platform is fully compatible with operation room (OR) environment and improves the light delivery and dosimetry in PDT. It can be adopted for diffusing optical tomography (DOT), spectroscopic DOT and fluorescent spectroscopy.

Keywords

Photodynamic therapy; light delivery; dosimetry; robotic platform

I. INTRODUCTION

Photodynamic therapy (PDT) is a treatment that uses a drug, also called a photosensitizer or photosensitizing agent, and a particular type of light. When photosensitizers are exposed to a specific wavelength of light, they produce a form of oxygen that kills nearby cells^[1–3]. Each type of photosensitizer can be activated by the corresponding light of a specific wavelength, which also determines how far the light can travel into the body. PDT treatment procedure

essentially has three steps. First, a light-sensitizing liquid, cream, or intravenous drug (photosensitizer) is applied or administered. Second, there is an incubation period of minutes to days. Finally, the target tissue is then exposed to a specific wavelength of light that can activate the photosensitizing medication.

PDT is currently used in a number of medical fields including oncology, dermatology and cosmetic surgery. In oncology, it is FDA approved for non-small cell lung cancer, esophageal cancer, and precancerous changes of Barrett's esophagus. Its use is also being further investigated through clinical trials in general oncology for conditions including cancers of the cervix, prostate gland, brain, and peritoneal cavity (the abdominal space that contains the stomach, liver, and internal organs). The prostate gland is also an organ that appears to be a good target for interstitial PDT. Tumors of the prostate are often confined to the prostate itself and brachytherapy techniques used for the placement of radioactive seed implants can be adapted for the placement of interstitial optical fibers.

For PDT dosimetry, the common approach is to measure the amount of photosensitizer administered to the patient and the amount of light delivered to the treatment area, but this approach has several problems. (a) The local concentration of photosensitizer varies from site to site in the body and from individual to individual. (b) The penetration of light into the target depends on the specific optical properties of that tissue. (c) If the tissue is hypoxic, or becomes hypoxic as a result of the PDT treatment, the yield of singlet oxygen – the principal mediator of biological damage in PDT – will be lower than expected. To complicate matters further, all of these parameters can change during treatment and each of the parameters can also influence the others. A successful dosimetry strategy must recognize and account for these variations.

The simplest clinical dose prescription for interstitial PDT is to quantify the total light energy emitted per length (J/cm) of the cylindrically diffusing fiber (CDF) for patients treated with a defined photosensitizer injection per body weight. In fact, the total fluence in tissues is a function not only of the incident light delivered by the laser but also of scattered light, so the clinical PDT treatments are prescribed in terms of the incident light delivered from the laser rather than the total fluence of light in the tissues. The incident light is a combination of scattered and incident light. Substantial differences in total fluence to tissues can be observed among patients if the clinician accounts only for incident light. Isotropic detectors are often used to measure the light fluence rate directly^[4]. These detectors have the advantage of detecting light from all directions, unlike flat photodiodes, which can only detect normally incident light^[5]. Dosimetry systems using isotropic light detectors have been developed to measure both incident and scattered light^[6], including multi-channel systems capable of recording light fluence rate in real-time at multiple sites. These systems begin to allow clinical researchers to measure and therefore prescribe a consistent total fluence to the tissues.

Diffuse optical tomography (DOT) is a noninvasive imaging technique in which light source and detectors are used to probe the interior of the body for oxygenation and other physiological changes. DOT systems use an array of detectors to sample as much reflected light as possible over the area of a surface, and then processing this information with

statistical models of photon transport to generate cross-sectional or 3-D images of the tissue. These images provide not only the structural data but also the functional information about the tissue, which can be derived from the typical absorption spectra of specific molecular species such as oxy- and deoxyhemoglobin. Typically, detectors placed close to the light source will detect light scattered from tissue just below the surface, while detectors placed further away will detect light from deeper tissue where the signal is very weak. Fluorescence techniques^[7, 8] can be used to quantify drug concentration and can provide valuable dynamic information relating to the photobleaching of the photosensitizer and oxygen consumption.

A compact robotic platform is designed for simultaneous multichannel motion for light delivery and dosimetry during interstitial photodynamic therapy (PDT), allowing arbitrary positioning of sources and detectors in 16 catheters. The characteristic of high speed and coordinating motion will make it possible to use short linear sources (e.g., 1- cm) to deliver uniform PDT treatment within reasonable time by source stepping optimization of multiple sources. Advanced robotic control algorithm handles the various unexpected circumstance. The robotic improves the light delivery and dosimetry in PDT. It can be adopted for diffusing optical tomography (DOT), spectroscopic DOT and fluorescent spectroscopy.

Measurement during PDT may be necessary if bleeding occurs and it is determined that the measured in-vivo light fluence rate deviates from the calculated light fluence rate. The advantage of this method is that optical properties can be measured rapidly during PDT using the CDF's already inserted in the treatment catheters. The alignment between the light source catheter and the detector catheter is not critical because the linear sources are positioned to illuminate the entire prostate, and the detectors can be scanned over its full length. Multiple motorized probes can be used to measure optical properties in different catheters simultaneously.

This robotic platform is an update of the one that has been successfully implemented in clinic to determine the optical properties in vivo quickly and reliably^[9]. We will use a computerized 16 channel attenuator system to deliver light sequentially to one of the CDFs and measure the light from all detectors (a minimum of 6 and a maximum of 9 detectors). The resolution of the prostate template is 5 mm and each scan resolution is 0.1 mm (for the current step motor system). Each scan per CDF can be completed in 2 seconds, resulting $2 \times 16 = 32$ seconds for all scans of 16 CDFs. This entire data acquisition procedure can be performed any time before, after, and during PDT if necessary.

II. ROBOTIC MULTI-CHANNEL PLATFORM DESIGN

Figure 1 shows the multichannel platform design (a) and prototype (b). It is a more compact, intelligent multi-channel platform, which is able to control each detector or light source individually. The outside dimensions of the platform are $30\text{cm} \times 12.8\text{cm} \times 2.5\text{cm}$. Movements of light sources and isotropic detectors are controlled by individual motors along different catheters. Each channel is designed with the positioning control to allow rigorous placement of light source/detector in the corresponding catheter. The 16

translational channels are arranged in parallel, so that the operator can easily monitor the light delivery procedure and manipulate the fiber holder.

Micro direct current (DC) motors (Micromo Co. 0816008S), each with high resolution optical encoder and precision gearhead, are adopted to drive the motions of the motion stage/fiber holder up to 16 channels independently. Each channel is constructed by precision lead screw and guide rod. The lead screw is supported at both ends with the bearings, and the motor is connected to the lead screw with helical beam flexible couplings. The motion of each channel has a resolution of 0.1 mm and a maximum speed of 5 cm/s. The travel range is 25cm. The special design for fiber holder is illustrated in Figure 2. The fiber holder can be easily attached and detached with the motion stage individually. The fiber holder design is interchangeable to be adaptable with the OR environment.

Figure 3 shows the control system for the motorized platform. Control system has a distributed scheme based on Ethernet network. The two 8 channel controllers (Galil motion Co. 2183) can talk with each other through the cross over Ethernet cable. Power supply provides $\pm 12V$ to the controller and amplifiers. The amplifier (Galil motion Co. 20341) is connected with the motion controller through the 96 pin slot interface. Each amplifier drives 4 DC motors. The control computer not only provides the interactive interface of operator and robotic platform, but also implements the optimal motion planning in PDT, DOT or fluorescence spectroscopy.

The individual translational channels can be combined according to different operational scheme with real-time optimal motion planning. Advanced robotic control algorithm handles the various unexpected circumstance in clinical procedure, e.g., position-torque/current control will be applied to prevent excessive force in the case of resistance in the fiber or motorized mechanism. Control software was developed to integrate with the optimal motion planning, DC motor control and the data acquisition of isotropic detectors as well as the spectrometer for fluorescence and absorption spectra measurements.

III. CALCULATION AND MOTOR SELECTION

1. Torque calculation

With the consideration of the mechanical transmission, friction and fiber resistance during the light delivery, the load of each fiber is equal to the 0.5N for the experience of previous clinical experiments [9]. The relevant coefficients are listed in table 1 according to the specifications.

The maximum torque is calculated by following the energy reservation:

$$k \cdot T \cdot \omega \cdot \eta_{Screw} \cdot \eta_{Gear} = L \cdot v \cdot \gamma \quad (1)$$

The maximum torque required from motor: $T = 0.5 \times 50 \times 2 / (2\pi \times 20 \times 0.7 \times 0.9 \times 4) = 0.158 Nmm$.

2. Speed and torque verification

The maximum speed of motor rotation is $20 \times 60 \times 4 = 4800 rpm$. According to the motor torque and speed curve in the Figure 4, the maximum output torque of the motor is around

0.26Nmm at the rotation speed 4800rpm, so the motor combined with 4:1 reduction ratio gearhead is powerful enough for our application.

3. Resolution and accuracy

The achieved resolution for translational motion is $pitch / (reduction\ ratio \times encoder\ line) = 0.012mm$. Considering the transmission clearance and fabrication quality, it can meet the design requirement on position accuracy, 0.1mm.

IV. ROBOTIC PLATFORM CONTROL

1. DC Motor model

DC motor model is illustrated in Figure 5. Equation (2) shows the electrical equilibrium, while equation (3) shows the mechanical equilibrium when DC motor is driving the motion stage.

$$v = R_a \cdot i + v_m + L_a \frac{di}{dt} = R_a \cdot i + K_b \frac{d\theta}{dt} + L_a \frac{di}{dt} \quad (2)$$

$$K_T \cdot i = T_L + B \frac{d\theta}{dt} \quad (3)$$

Combine (2) and (3), the motor model equation is obtained as (4). It is a second order differential equation.

$$v = \frac{L_a \cdot B}{K_T} \frac{d^2\theta}{dt^2} + \left(\frac{R_a \cdot B}{K_T} + K_b \right) \frac{d\theta}{dt} + R_a \cdot \frac{T_L}{K_T} \quad (4)$$

Where, v is the terminal voltage applied to the motor, θ the rotational output angle in rad, i is the armature current, R_a the armature winding resistance, B is the viscous friction coefficient. K_b is the motor back emf constant, K_T is the motor torque constant, L_a is the rotor inductance, T the load torque on motor shaft.

Equations (2) and (3) can also be transformed into (5) and (6) by using Laplace transformation. The hierarchical chart of DC motor model is shown in Figure 6.

$$i(s) = \frac{v(s) - K_b s \theta(s)}{R_a + L_a s} \quad (5)$$

$$\theta(s) = \frac{K_T i(s) - T_L(s)}{B s} \quad (6)$$

The parameters above are listed in the table 2 according to the specification of DC motor.

2. Open-loop motor control

By using Matlab Simulink (Math Works Co.), the DC motor modeling and simulation for open-loop control were performed (See Figure 7). It is composed of the load module, the DC motor model and the input source.

If the step source of input is 8V, the response of motor within 0.005s is shown in Figure 8. The load in the simulation of the motor open-loop control is a constant, 0.26 Nmm, that is to say the load TL signal is only used. The time of simulation is 0.005s. The DC motor shows very good characteristics for dynamic response in the open-loop control simulation.

3. Close-loop motor control

The close-loop control of DC motor is simulated using PID controller with approximate derivative, see Figure 9. The transfer function of the PID controller with approximate derivative is expressed by Figure 10. The close-loop control is based on the position feedback of the optical encoder coupled with DC motor.

The step source of input position is 100 rads. With the constant load, the response of motor close-loop within 0.2s is shown in Figure 11. Figure 12 shows the response of the close-loop control, with the simulation of variable load of mechanical transmission, friction and fiber resistance during the light delivery. Set PID parameters as follows, $K_p = 100$, $K_i = 0.05$, $T_d = 1$, and $N = 100$.

The close-loop control of DC motor based on position feedback is rapid, stable and accurate. It also shows the good robust capability for the variable load caused by mechanical transmission, friction and fiber resistance during the light delivery in clinical application. The position-torque/current control algorithm will be applied to prevent excessive force in the case of resistance in the fiber or motorized mechanism.

V. DISCUSSION AND CONCLUSION

The robotic platform performs light delivery and dosimetry independently. With the capability of allowing arbitrary positioning of light sources and detectors in each catheter, the pre-alignment can be easily achieved for the profiles of each scan (Figure 13). 16 compact translational channels can be also combined according to different operational scheme with real-time optimal motion planning, to greatly reduce the treatment or dosimetry time (Figure 14). The characteristic of high speed and coordinating motion will make it possible to use short linear sources to deliver uniform PDT treatment to a bulk tumor within reasonable time by source stepping optimization of multiple sources Simultaneously.

In the future, the accuracy and stability of the platform will be verified with testing experiments. Advanced robotic control algorithm with position-torque/current control will be applied to prevent excessive force in the case of resistance in the fiber or transmission mechanism. The robotic multichannel platform can also be adopted for diffusing optical tomography (DOT), spectroscopic DOT and fluorescent spectroscopy.

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Figure 1.

(a) Schematics of multichannel platform design and (b) Prototype of the platform with one channel assembled

Figure 2.
Fiber holder design

Figure 3.
Scheme of control system

Figure 4.
Speed and torque curve for the DC motor

Figure 5.
Illustration for DC motor model

Figure 6.
Hierarchical chart of DC motor model

Figure 7.
DC motor model using Simulink

Figure 8.
Open-loop control simulation with constant load

Figure 9.
DC motor close-loop simulation based on PID controller

Figure 10.
Illustration of PID controller with approximated derivative

Figure 11.
Close-loop control simulation with constant load

Figure 12.
Close-loop control simulation with variable load

Figure 13.
Pre-alignment for the scanning profiles

Figure 14.
Operational scheme with real-time optimal motion planning

Table 1

Specification for torque calculation

Efficiency of Mechanism η_{Screw}	70%
Gearhead ratio: k	4:1
Efficiency of gearhead transmission: η_{Gear}	90%
Motion speed: v	50mm/s
Screw rotation velocity: $\omega = 2\pi \cdot v / pitch$	1200rpm

Table 2

Parameters of DC motor model

R_a	75.7 Ohm
B	4.85×10^{-8} Nm/A
K_b	4.1×10^{-3} V/rad/s
K_T	4.1×10^{-3} Nm/s
L_a	3.1×10^{-4} H