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Nanorobots for Laparoscopic Cancer Surgery

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Abstract

This paper presents an innovative hardware architecture for medical nanorobots, using nanobioelectronics, clinical data, and wireless technologies, as embedded integrated system devices for molecular machine data transmission and control upload, and show how to use it in cancer surgery. The integration of medical nanorobotics and surgical teleoperation has the use of robotic laparoscopy concepts. To illustrate the proposed approach, we applied advanced 3D simulation techniques as a practical choice on methodology for molecular machine integrated system analyses and biomedical instrumentation prototyping.

Keywords: Architecture, cancer, hardware, integrated circuit, medical nanorobotics, nanobioelectronics, nanomechatronics, nanomedicine, surgical instrumentation, VLSI.

1. Introduction

Nanorobots are expected to provide advances in medicine through the miniaturization from microelectronics to nanoelectronics. This work presents a nanorobot architecture based on nanobioelectronics [4] for the gradual development and future use of nanorobots to cancer surgery. Cancer can be successfully treated with current stages of medical surgery tools. However, a decisive factor to determine the chances for a patient with cancer to survive is: how precise can the surgeon eliminate malignant tissues from the patient's body. Preoperative lymph node staging with computerized tomography or magnetic resonance imaging (MRI) has been disappointing since sensitivity and specificity are limited [13]. The success of Retroperitoneal Lymph Node Dissection (RPLND) is directly related with determining areas associated with tumor cell invasion. Nanorobots can provide information for the surgeons to deal with the medical procedure precisely mapping the target areas requiring dissection. The nanorobot capability to detect cancer targets is demonstrated through extensive analyses. The conclusions for the proposed model are obtained with real time 3D simulation based on clinical parameters.

2. Robotic Laparoscopy

Laparoscopy has some different robotic systems currently in use [14], [21]. A laparoscopic system can use voice (or pedal) control to direct the movements of a robotic arm. The arm usually holds a laparoscope, although it may alternatively hold a laparoscopic retractor. A preprogrammed voice card that allows the device to understand and respond to the surgeon commands is normally used. Laparoscopic images are steadier, with fewer camera changes and inadvertent instrument collisions than an inexperienced human assistant [14]. It has proved very popular for procedures such as laparoscopic radical prostatectomy and laparoscopic pyeloplasty. As an example, the daVinci Surgical System [10] has been responsible for

Fig. 1. A daVinci robot at Guy's Hospital.

the huge surge in the number of robotic procedures performed in the past 5 years [21]. Robotic prostatectomy now accounts for over 10% of radical prostatectomies performed in the USA, a proportion that is increasing year on year [21].

The daVinci is the most advanced master–slave system developed until now (Fig. 1). The basic principle involves control of three (or four) robotic arms by a surgeon sitting at a console. The system has three components: (a) a surgeon console, (b) a patient-side cart and (c) an image-processing or insufflation stack. In our work, the proposed approach includes the analyses of the additional component: (d) nanorobots.

Console: The surgeon controls the robot from a console placed away from the operating table. The three-dimensional view from the endoscope is projected in the console at 610 magnification. The surgeon's thumb and forefinger control the movements of the robotic arms. Foot pedals allow control of diathermy and other energy sources. Motion scaling enhances the elimination of tremor, allowing very smooth and precise movements.

Patient-side cart: The robotic arms are mounted on this cart, one of which holds the high-resolution three-dimensional endoscope.

Image-processing/insufflation stack: The stack contains the camera-control units for the three-dimensional imaging system, image-recording devices, a laparoscopic insufflator and a monitor allowing two-dimensional vision for the assistants. Current laparoscopic instrumentation allows only 4 df. However, the daVinci Surgical System provides a 7 df that the human wrist normally enjoys, making complex laparoscopic procedures smooth. The three-dimensional vision, enhanced magnification and motion scaling all make life a little easier for the operating surgeon.

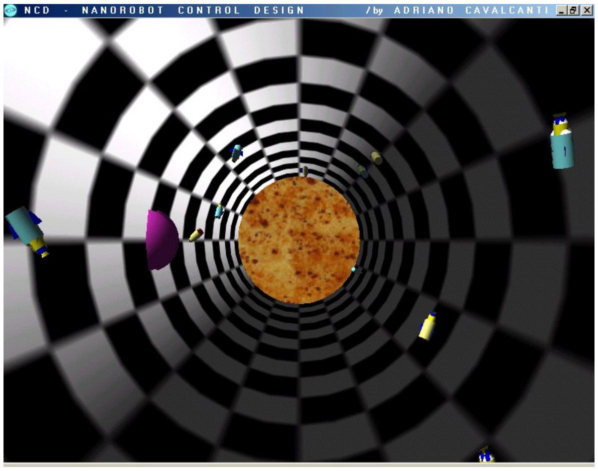

Fig. 2. All nanorobots swim near the wall to detect E-cadherin signals. Vein internal view without the red cells. The tumour cell is the target represented by the pink sphere located left at the wall.

Nanorobots: for the surgery procedures, the nanorobots are used as integrated tools with embedded high precision transducers for mapping specific areas requiring dissection (Fig. 2). During the surgery, they can helps to locate medical targets reporting tumor cell invasion, saving time and improving productivity. Real time additional measurement based on chemical patterns established to be monitored from the surgeons can also be provided.

3. Nanorobot for Laparoscopy

The main parameters used for the medical nanorobot architecture for surgery, its control activation, as well as the required technology background that may lead to manufacturing hardware for molecular machines, are described next.

3.1. Manufacturing Technology

The ability to manufacture nanorobots may result from current trends and new methodologies in fabrication, computation, transducers and manipulation. CMOS VLSI design using deep ultraviolet lithography provides high precision and a commercial way for manufacturing early nanodevices and nanoelectronics systems [28]. To validate designs and to achieve a successful implementation, the use of VHDL (Verification Hardware Description Language) has become the most common methodology utilized in the integrated circuit (IC) manufacturing industry [15].

3.2. Chemical Sensor

Through the use of nanowires, existing significant costs of energy demand for data transfer and circuit operation can be decreased by up to 60% [28]. CMOS-based sensors using nanowires as material for circuit assembly can achieve maximal efficiency for applications regarding chemical changes, enabling new medical applications [29]. Nanosensor manufacturing array processes can use electrofluidic alignment to achieve integrated CMOS circuit assembly as multi-element systems [28]. Passive and buried electrodes can be used to enable cross-section drive transistors for signal processing circuitry readout. The passive and buried aligned electrodes must be electrically isolated to avoid loss of processed signals.

New materials such as strained channel with relaxed SiGe layer can reduce self-heating and improve performance [3]. Recent developments in 3D ICs and FinFETs double-gates have achieved astonishing results and according to the semiconductor roadmap should improve even more. To further advance manufacturing techniques, Silicon-On-Insulator (SOI) technology has been used to assemble high-performance logic sub 90nm circuits [24]. IC design approaches to solve problems with bipolar effect and hysteretic variations based on SOI structures has been demonstrated successfully [3]. Thus, already-feasible 90nm and 45nm CMOS devices represent breakthrough technology devices that are already being utilized in products.

3.3. Power Supply

The use of CMOS for active telemetry and power supply is the most effective and secure way to ensure energy as long as necessary to keep the nanorobot in operation. The same technique is also appropriate for other purposes like digital bit encoded data transfer from inside a human body [20]. Thus nanocircuits with resonant electric properties can operate as a chip providing electromagnetic energy supplying 1.7 mAat 3.3V for power, allowing the operation of many tasks with few or no significant losses during transmission [27]. RF-based telemetry procedures have demonstrated good results in patient monitoring and power transmission with the use of inductive coupling [7], using well established techniques already widely used in commercial applications of RFID [26].

A practical way to achieve easy implementation of this architecture will obtain both energy and data transfer capabilities for nanorobots by employing mobile phone in such process [1]. The cell phone should be uploaded with the control software that includes the communication and energy transfer protocols.

3.4. Data Transmission

Work with RFID (Radio Frequency Identification Device) has been developed as an IC device for medicine [26], [27]. Using integrated sensors for data transfer is the better answer to read and write data in implanted devices. Teams of nanorobots may be equipped with single-chip RFID CMOS based sensors [23]. CMOS with submicron SoC design could be used for extremely low power consumption with nanorobots communicating collectively for longer distances through acoustic sensors. For the nanorobot active sonar communication frequencies may reach up to 20µW@8Hz at resonance rates with 3V supply [12].

More widely accepted and usual than an RF CMOS transponder, cell phones can as alternative be extremely practical and useful as sensors for acquiring wireless data transmission from medical nanorobots implanted inside the patient's body. Such phones can be a good choice to control upload interface for medical nanorobots application in drug delivery, patient monitoring, tracking and early detection of malignant tissues in cancer, and in other kinds of biomedical problems. To accomplish that, chemical nanosensors may be embedded in the nanorobot to monitor E-cadherin gradients [25]. Nanorobots may be programmed to make a detailed screening of the patient whole body.

Frequencies ranging from 1 to 20MHz can be successfully used for biomedical applications without any damage [27]. A small loop planer antenna working as an electromagnetic pick-up with a good matching to the Low Noise Amplifier is used with the nanorobot [4].

4. System Implementation

Real time 3D prototyping and simulation are important tools for nanotechnology development. Such techniques have significantly helped the semiconductor industry to achieve faster VLSI development [28]. It may have similarly direct impact on the implementation of nanomanufacturing techniques and also on nanoelectronics progress. Simulation can anticipate performance [5] and help in new device design and manufacturing, nanomechatronics control analysis [6] and hardware implementation [4], [24].

The nanorobot design includes integrated nanoelectronics [28]. The nanorobot architecture involves the use of RF tracking back information about E-cadherin levels for medical instrumentation, temperatures, and cancer target detection for laparoscopy surgery [1], [26], [21]. The nanorobot uses a RFID CMOS transponder system for in vivo positioning [8], [26], using well established communication protocols which allow track information about the nanorobot position [1].

The simulation includes the NCD (Nanorobot Control Design) software for the nanorobots interactive operation [18]. The nanorobot exterior shape consists of a diamondoid material [22], to which may be attached an artificial glycocalyx surface [19], that minimizes fibrinogen (and other blood proteins) adsorption and bioactivity, ensuring sufficient biocompatibility to avoid immune system attack [8], [9]. Different protein types are distinguished by a series of chemotactic sensors whose binding sites have a different affinity for each kind of biomolecular structure [8], [17]. These sensors can also detect obstacles which might require new trajectory planning [6].

5. Chemical Signals

Our research aims to demonstrate how to apply nanorobots for laparoscopic cancer surgery. We examine the nanorobot sensing for the simulated architecture in detecting gradient changes on E-cadherin protein signals [25]. Thus, we improve the response by having the nanorobots maintain positions near the vessel wall instead of floating throughout the volume flow in the vessel (Fig. 2). In the render modelling was used a vein wall with grid texture to enable better depth and distance perception in the 3D workspace. A key choice in chemical signaling is the measurement time and detection threshold at which the signal is considered to be received [11]. Due to background concentration, some detection occurs even without the target signal. As a guide for the choice of threshold, we use the diffusive capture rate α for a sphere of radius R in a region with concentration as:

$$\alpha = 4\pi DRC \tag{1}$$

where the concentration for other shapes such as cylinders are about the same [2], [11]. With independent random motions for the molecules, detection over a time interval Δt is a Poisson process with mean value $\alpha \Delta t$. When objects occupy only a small fraction of the volume the velocity at distance r from the center of the vessel is:

$$w = 2v(1 - (r/(d/2))^2) \tag{2}$$

and with the cells, the velocity shows somewhat a parabolic flow [8], but similar enough for this parabolic profile to give a useful design guideline.

After the first nanorobot has detected a tumor for medical treatment, it can be programmed to attach on it. Therefore, the system instrumentation has enough time to make a precise mapping on any possible area requiring dissection, providing information even about a tiny prostatic nodule inside small venule vessels [25], [13].

Similarly to quorum sensing in bacteria, from monitoring the concentration of signals, chemical substances for near communication can attract or repeal nanorobots, and permit to estimate the number of how many are at the target. However to detect multiple different chemicals requires additional sensors for more than one chemical. Also, producing chemicals for communication, or transporting it to release in the blood stream when required, can demand considerably energy and critical space for a nanorobot that must stay fit, in order to be useful for medicine. The best choice for nanorobot communication is to apply differentiated signals using an electromagnetic ultrasound CMOS transducer [16], which may enable other nanorobot to come together to help, or simply stay away. The nanorobots should be concentrated in a tumor plaque, or for controllable chemotherapy, or for precise mapping purposes in a surgical dissection.

The surgeon can determine the amount of nanorobots to concentrate per lymph node. The amount of nanorobots for target can change depending on the stage of cancer, the tumor size, and can be defined by the oncologist according with the information retrieved from the nanorobots through RF electromagnetic waves. Once defined the best strategy for each case, sending this information back may leave the other nanorobots free to continue detecting further malignant tissues bounding the surgery area. Thus, it may be extremely useful to control tumor cell invasion and cancer metastasis. For investigation purposes, values of $N=\{50\}$ were set up in the simulator as a reasonable amount of nanorobots for the plaque target lesion.

6. Numerical Results

In our study 50 nanorobots perform similar tasks on detecting and acting upon medical targets demanding surgical intervention. Each nanorobot is programmed to move through the workspace being teleoperated from the surgeons. The fluid flow pushes the

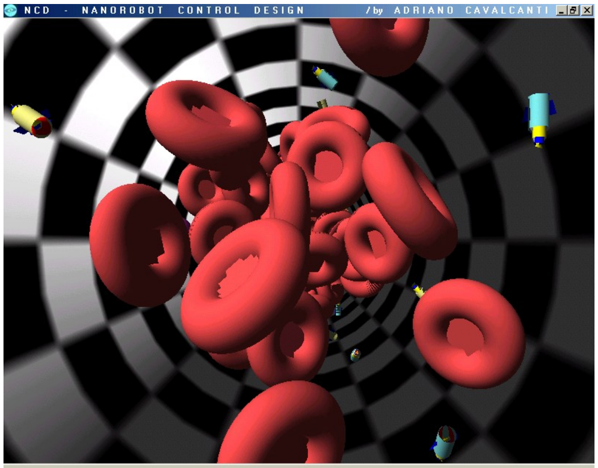

Fig. 3. View of simulator workspace showing the vessel wall, cells and nanorobots.

concentration of the diffusing signal downstream. Consequently a nanorobot passing more than a few microns from the source won't detect the signal while it is still relatively near the source. As an example, the first nanorobot passing close a lymph node may on average detect the higher signal concentration within about 0.16s. Thus, keeping their motion near the vessel wall, the signal detection happens after these have moved at most $10\mu m$ past the source. Therefore, it provides about 6nanorobot/s arriving at the tumor cell in the small venule. Nanorobots passing within $\approx 0.1\mu m$ of the target usually bump into it. Those passing within a few microns often detect the signal, which spreads a bit further upstream and away from the single tumor due to the slow fluid motion near the venule's wall and the cells motion. Thus, the present 3D simulation provides guidelines for nanorobot communication and activation control, as well as for sensor manufacturing design.

Distinct performances were observed throughout a set of analyses obtained from the NCD software, where the nanorobots use also electromagnetic ultrasound transducers as the communication technique to interact dynamically with the 3D environment, and to achieve a more successful collective coordination. Fig. 3 shows the virtual environment in our study, comprised a small venule which contains nanorobots, the red blood cells (RBCs) and a single tumor cell, which is the target area on the vessel wall. Here, the target area is overleaped by the RBCs. In the simulation, the nanorobots search for possible small cancer tumor into the workspace crowded by RBCs, transmitting back information for the surgeons. In Fig. 4 it could be observed in a detailed fashion the information about the nanorobots behaviors. It shows the time required for 50 nanorobots to identify and reach the target in different vessels diameters. If every nanorobot passing through the vessel found the target, 50 nanorobots would arrive at the target in about 0.9s. The average and standard deviation of time were measured in seconds to get 50 nanorobots with their respective targets for the results describing vessels with different diameter sizes (Fig. 4). Comparing different venule sizes, the nanorobots can manage to reach the targets more efficiently demanding less time when the vessel diameters are proportionally smaller.

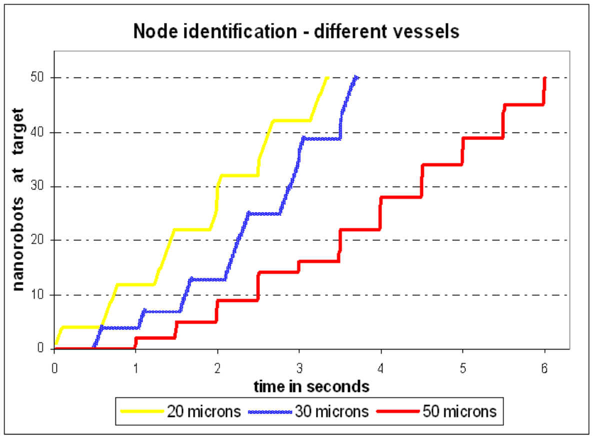

Fig. 4. The time required for nanorobots to achieve the targets in vessels with different diameters.

7. Conclusion

The development of nanorobots may provide remarkable advances for surgery and treatment of cancer. Using chemical sensors they can be programmed to detect different levels of E-cadherin and beta-catenin and help surgeons for a better sensing and manipulation in laparoscopy. Our work has shown a comprehensive methodology on using nanorobots for medical surgical procedures. The simulation has demonstrated how the medical conditions and vessel sizes can interfere directly in the nanorobot actuation. This approach can be useful for surgeons sensing medical targets with high precison at nanoscopic levels. Therefore, nanorobots may provide useful tools in biomedical instrumentation for hard task of isolating and defining the exact mapping of cancer tissues, and to demark areas with possible tumor cell invasion.

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