An In-Body Wireless Communication System for Targeted Drug Delivery: Design and Simulation

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Abstract— **Statistics show that the figure of new cancer cases and deaths reported each year are increasing considerably. The current situation demands an efficient targeted drug delivery system that enables localized drug administration which can be externally controlled. This paper proposes a remotely triggered targeted drug delivery system that is capable of providing drugs to multiple patients in a periodic basis and works according to the instructions transmitted from the external transmitter module. We present the characteristics and challenges in the propagation of Radio Frequency (RF) signals through different body tissues from the perspective of targeted drug delivery system so that the analysis can lead to the selection of optimum frequency needed for in-body communication. This paper focuses on the design of an implantable drug delivery system, based on the optimum frequency obtained from the simulation results.**

Keywords— Targeted drug delivery system; wirelessly controlled; RF characteristics; optimum frequency range

I. INTRODUCTION

According to cancer statistics of GLOBOCAN, the number of cancer cases reported in the world reached to 12.7 million. Of these reported cases, 6.6 million were men and 6.0 million were women. Most likely this statistics is anticipated to increase to a large number in the coming years. Hence there is an urgent need for an efficient drug delivery system with no side effects. A good solution to this is the adoption of an implantable targeted drug delivery device.

A large amount of research and money go into the approval and marketing of drugs, but the sad fact is that many of these medicines do not frequently reach diseased site. Furthermore, these treatment methods have many side effects such as nausea and vomiting, hair loss, bone marrow changes, fertility problems, memory changes etc.

The potential to provide controlled dosage of a drug to a confined site (affected site) is necessary. The harmful effects related with systemic medication can be reduced by the delivery of medicines in a controlled way at the target site. In targeted drug delivery system, necessary amount of medicines can be given to the affected area in a highly localized form so that the drugs will not influence the normal body cells. A targeted drug delivery system consists of an RF-enabled device or a transceiver for short range, reliable, in-body communication. This technology is an efficient one with different uses in invasive information technology.

The primary aim of the work is to examine the challenges related with developing a remotely triggered targeted drug delivery system and to propose a design for a wirelessly controlled targeted drug delivery system. The main challenges include the study of path loss in different body parts and the frequency range suitable for in-body communication in different target sites. Knowledge of RF propagation for in-body communication is helpful for better performance and design of physical layer. RF propagation characteristics are collected by conducting experiments, measuring and processing the obtained data to get channel information and characteristics. But conducting experiments for in-body communication is not an easy task since it involves many complexities due to dielectric property variation and thickness variation of body tissues.

This paper, therefore presents a simulation for analyzing the complexities in body cells by taking into account the path gain and optimum frequency for communication in various body tissues.

The work estimates the characteristics of different body tissues. The main objective of the analysis is a fair comparison of different contexts such as propagation through blood, fat, muscle etc.

Section II includes related works. Section III and IV describes about the design and architecture of targeted drug delivery system. The challenges involved in in-body wireless communication are described in section V. The results obtained from MATLAB simulation are given in section VI.

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II. RELATED WORKS

Smith et al. [1] describes the development of an implantable system designed to deliver daily drug doses in a controlled manner over a specific duration of time. The key ideas discussed were the physical size of the device, the power consumption and capability for wireless communications to enable external control. Wireless power transfer which is the main design parameter removes the need for a battery. The system was designed for 7MHz but the reason behind selecting that particular frequency was not addressed. However we need to analyze all possible frequencies so that the optimum frequency can be selected for in-body communication.

Sayrafian et al. [2] describes about propagation media involved in in-body communication. They created an environment, to watch RF propagation from implanted device inside a human body. They showed the variation of path gain in accordance with distance and shadowing but the paper is not addressing the variation of path gain with respect to frequency and dielectric properties.

Takizawa et al. [3] developed a channel model by considering path loss and power delay profile obtained from channel transfer functions. But the model did not address the issues and path loss for implantable devices.

Taparugssanagorn et al. [4] took some scenarios and made UWB Body Area Network measurements to study the behavior of RF signals in body, but they only considered 3-11GHz frequency range.

Rehimi et al. [5] explains about a drug delivery system that works on the principle of resonance between a transmitter and receiver. The work concentrated mainly on the fabrication of the device.

Grayson et al. [6] used MEMS technology for drug delivery devices. The microchip developed for drug delivery was capable of delivering drugs in a controlled manner.

Poon et al. [7] studied the range of frequencies by considering the tradeoff between tissue absorption and received power by making experimental models of body parts.

Most of the above mentioned work concentrated on particular frequencies but the clear idea behind the selection of these frequencies is unknown. Also, the dielectric property variation of tissues needs to be considered while designing an implantable system.

III. OVERVIEW OF TARGETED DRUG DELIVERY DEVICE

An externally controlled targeted drug delivery device consists of a transmitter which can be placed in the room of the patient. Transmitter that controls the implanted device consists of some switches or buttons. The implanted device is the receiver module of the system which consists of different small sized drug reservoirs that is filled with specific amount of medicines. When a key in the transmitter is pressed, the digital information corresponding to the pressed key which is the address of the required reservoir is wirelessly transmitted to the receiver placed inside the body. Receiver decodes the information and address corresponding to a particular drug reservoir is obtained. Then it triggers the particular drug reservoir and medicine is delivered to the site by opening the capsule.

IV.ARCHITECTURE

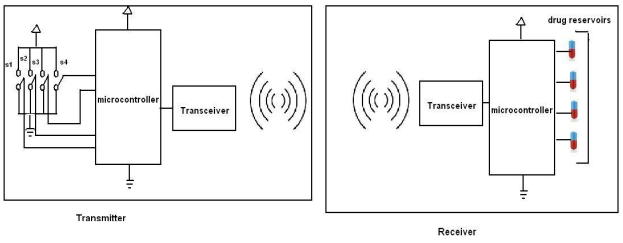

Figure 1: Architecture Diagram for Targeted Drug Delivery

Figure 1 shows the architecture diagram of wireless communication in targeted drug delivery system. The transmitter consists of a group of switches, a microcontroller, and a wireless transceiver. Each switch in the transmitter corresponds to different drug reservoirs in the receiver. When a switch is pressed, corresponding signal which has the information regarding the address of the reservoir is transmitted across a wireless link. Receiver consists of an RF enabled device that is a transceiver, a microcontroller and multiple drug reservoirs carrying different drugs. The receiver part of the system which is placed inside the body receives the information and corresponding drug reservoir opens to release the drug.

The architecture supports two way communications and thus the device assures reliable communication. A provision of feedback from the receiver to the transmitter can improve the efficiency of the system by providing acknowledgement regarding the opening and closing of drug reservoirs in the receiver.

V. CHALLENGES IN IN-BODY COMMUNICATION

The complexities involved in developing an implantable drug delivery system mainly include the attenuation that is varying according to the environment

through which it travels. In Fig 2, as the signal propagates through different layers of body tissues such as skin, fat, muscle etc, the attenuation varies dynamically as the nature of tissue changes.

Another factor that varies with respect to body tissues are dielectric properties. All these factors will affect the path gain which in turn affects the selection of optimum frequency.

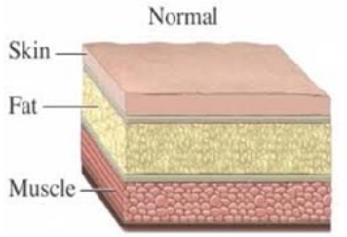

Figure 2: Layered structure of body tissues [17]

A. Attenuation in Body Tissues

Attenuation through body varies dynamically as the signal travels through different body tissues**.** Attenuation coefficients are used to analyze different media according to how strongly the transmitted signal strength decreases as a function of frequency. The attenuation coefficient can be used to determine total attenuation in various body tissues using the equation:

Attenuation in dB=α [dB/(MHz.cm)].l(cm).f(MHz) (1)

Where α is the attenuation constant

l is the medium length

f is frequency

As this equation shows, in addition to the dependence on the medium length and attenuation coefficient, attenuation varies linearly with respect to the frequency of the signal. Attenuation coefficients and medium length (average thickness) usually vary for different media and thus the attenuation varies dynamically. Studies show that bimolecular environment and water are mediums with high attenuation. The attenuation coefficients of body tissues are listed below.

Table1: Attenuation Constants of Body Tissues [15]

Body tissue	A(Attenuation Constant)
Blood	0.2
Bone	6.9
Fat	0.48
Muscle	1.09
Cardiac	0.52

B. Dielectric Properties of Body

Dielectric properties of various body tissues and biological fluids vary dynamically with respect to frequency. The properties considered are the frequency variations of the permittivity and electrical conductivity. The electrical properties of various tissues and blood and also the differences between non affected and cancerous tissues are available. Some of the physiological and biophysical processes are responsible for the dielectric property variation of body tissues.

Permittivity is measured by the capability of a body tissue to polarize in the presence of a field. Permittivity changes for different body tissues which in turn affects path gain experienced by the signal.

The permittivity of a medium is given by [16]

$$\varepsilon = \frac{\sigma}{(\varepsilon_0 \omega)} \qquad (2)$$

where σ is the conductivity of the medium

ε_0 is the permittivity of free space

ω is the angular frequency

Electrical conductivity is a measure of a material's ability to conduct an electric current.

C. Path Gain in Body

Communication inside a human body is hindered as a result of attenuation and absorption. A path loss or path gain model helps to analyze various losses inside the body. This work studies the path gain experienced in different body tissues. A typical path gain model can be developed based on near field behavior since the communication range for implantable devices are much less. In near field behavior, short range communication path gain is given by [9]

Path gain =

$$\frac{P_r}{P_t} = \left(\frac{G_{TX}.G_{RX}}{4}\right)\left[\left(\frac{1}{(kd^2)}\right) - \left(\frac{1}{(kd)^2}\right) + \left(\frac{1}{(kd)^6}\right)\right] \qquad (3)$$

where $k = \frac{2\Pi}{\lambda}$

P_R is the received power

P_T is the transmitted power

G_{TX} is gain of transmit antenna

G_{RX} is gain of receive antenna

d is the distance between transmitter and receiver

Since the analysis is based on frequency and dielectric properties of body tissues, we expressed path gain with respect to these parameters.
k can be replaced in terms of frequency which in turn relates to dielectric properties i.e. $f = \left(\frac{\sigma}{2\pi\varepsilon\varepsilon_0} \right)$ (4)

So Path gain =

$$\frac{P_{RX}}{P_{TX}} = \frac{G_{TX}.G_{RX}}{4}\left[\left(\frac{c}{(2\pi fd)^2}\right) - \left(\frac{c}{(2\pi fd)^4}\right) + \left(\frac{c}{(2\pi fd)^6}\right)\right]$$

$$= \frac{G_{TX}, G_{RX}}{4}\left[\left(\frac{c}{\left(\left(\frac{\sigma}{\varepsilon\varepsilon_0}\right)d\right)^2}\right) - \left(\frac{c}{\left(\left(\frac{\sigma}{\varepsilon\varepsilon_0}\right)d\right)^4}\right) + \left(\frac{c}{\left(\left(\frac{\sigma}{\varepsilon\varepsilon_0}\right)d\right)^6}\right)\right] \quad (5)$$

VI. SIMULATION RESULTS

Simulation is done to analyze the signal propagation through different body tissues. By analyzing the path gain in body tissues it is possible to select an optimum frequency range for in-body communication in different body tissues. The simulation also considers the dielectric property variation of tissues also. By varying frequency and distance between transmitter and receiver, path gain in different medium is studied. Results obtained from Simulation done using MATLAB 2011a are discussed in the sections below.

A. Attenuation vs. Frequency

Attenuation in different body tissues can be calculated using (1) by giving frequency, attenuation coefficients and medium length (average thickness) for different body tissues as input parameters.

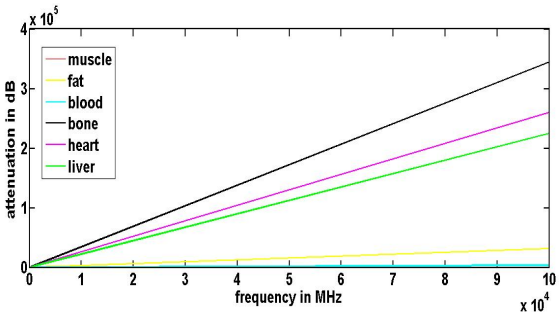

Figure 3: Attenuation vs. Frequency

Fig 3 shows the variation of attenuation vs. frequency in different body parts. These simulations showed attenuation in different body tissues such as muscle, fat, blood, bone, heart, liver etc. Analysis of the figures showed that attenuation is more in bone and less in blood. So a special attention must be taken while designing the system if it is implanting in bone. The effect of attenuation only comes into the picture at higher frequencies (above 1 GHz).So GHz range frequency cannot be used for in-body communication.

B. Path Gain vs. Frequency in Blood

Path gain in blood corresponding to different frequencies from 10 Hz to 100GHz can be calculated for different distances using (5). The 10 Hz -100GHz frequency range is taken since the path gain variation could be analyzed for such a high range of frequencies.
Assumptions taken: G_{tx} and G_{rx} equal to 0.5
Normally the distance between transmitter and receiver is small for implantable devices. So the distances are taken in the range 2.5cm to 30cm since our work is referring to short range communication.

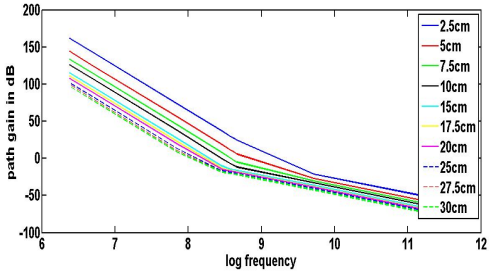

Figure 4: Path Gain in Blood

Fig 4 shows the variation of path gain in blood with respect to the frequency for different distances. In blood, path gain varies from 170dB to -70dB. Results showed that lower frequencies suffer less path loss. Typical path gain corresponding to in-body communication is -40dB to -10dB. So optimum frequency range observed for corresponding path gain is 200-800MHz (frequencies in GHz range are avoided due to attenuation).

C. Path Gain vs. Frequency in Fat

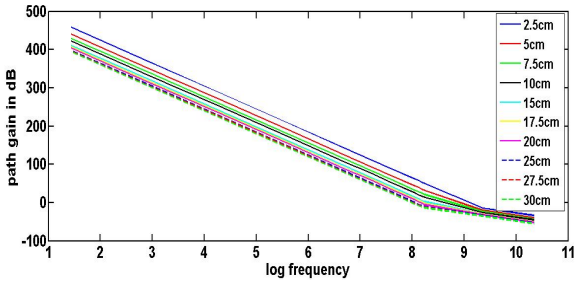

Figure 5: Path Gain in Fat

Fig 5 shows the variation of path gain in fat with respect to the frequency for different distances. In fat, path gain varies from 470dB to -70dB. Lower frequencies suffer less path loss and the optimum frequency range observed corresponding to -40 to - 10dB is 200-800MHz

D. Path Gain vs.Frequency in Muscle

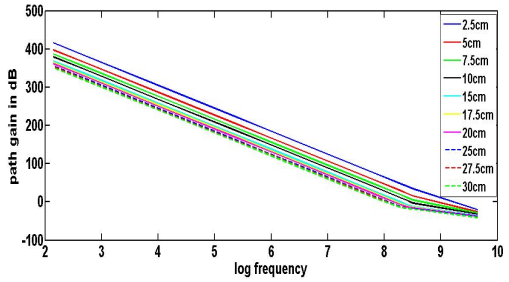

Figure 6: Path Gain vs. Frequency in Muscle

Fig 6 shows that path gain is varying from 420dB to --40dB dB. Frequency can be selected in the range 200MHz-800MHz corresponding to the path gain -40 to -10dB. If there is a need for a specific path gain (say -30dB,-35dB), the corresponding frequency can be selected from the plot.

E. Path Gain vs. Frequency (Skin->Fat->Blood->Muscle)

When the signal enters the body, it passes through different layers such as skin, fat, blood, muscle etc. As the dielectric properties varies, path gain changes accordingly in these tissues. This effect can be analyzed by taking the dielectric properties of these tissues separately in (5).

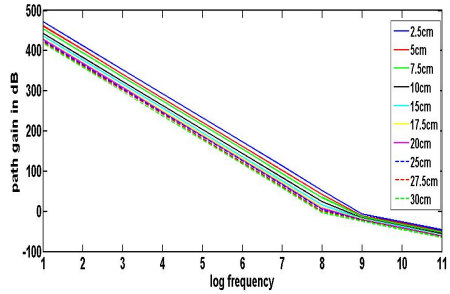

Figure 7: Path Gain vs. Frequency in Skin->Fat->Blood->Muscle

Here also path gain varies from 470dB to -70dB. Frequency range needed for the design of the hardware can be selected according to the specification of the application.

F. Comparison of Path Gain in Free Space and Body-Effect of Far Field and Near Field

A comparison of path gain in body and free space is necessary in order to analyze the degradation of path gain in body tissues. Distances from 10 to 80cm (since we only consider short distance between the transmitter and the receiver) are taken for evaluation. By assuming that the signal enters into the body at 65 cm, an analysis is done for a fair comparison between the two.

Dielectric properties of muscle are taken for the analysis and plotted path gain against distance using (5)

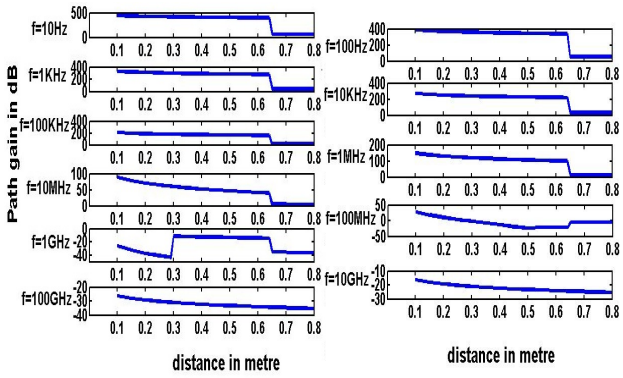

Figure 8: Effect of near field and far field in body and free space

The effect of far field is visible only at higher frequencies i.e. 1-100 GHz. Fig 8 shows that, for 1 GHz, far field comes into picture at a distance greater than or equal to 30cm. For 10 GHz and 100GHz, effect of far field is visible at all distances.

The inferences obtained from the analysis are:

i) More attenuation is experienced in bone than in blood.

ii) Higher frequencies (GHz range) cause more attenuation and hence these frequencies are eliminated.

iii) The results of path gain analysis showed that the optimum frequency range suitable for in-body communication in almost all tissues considered is from 200-800MHz.

CONCLUSION

Our work analyzed the challenges associated with developing a remotely triggered targeted drug delivery system and proposed a design for a wirelessly controlled targeted drug delivery system that can control drug delivery externally. We simulated and analyzed characteristics of RF propagation through body tissues such as skin, fat, muscles, blood, and bone. The RF characteristics were analyzed with respect to the average thickness of body tissues, dielectric properties like permittivity and conductivity, attenuation etc. The results of

the simulation contributed to the selection of the optimum frequency range. Path gain experienced as the signal traverse through different body tissues was analyzed. The optimum frequency range needed for in-body communication can be selected corresponding to the typical path gain demanded by the application. Since frequencies in GHz range suffer more attenuation, it is not preferred for communication. Since the lower frequencies suffer more attenuation, it is not suitable for short range communication. So the optimum frequency range always lies above 100MHz and below 1 GHz. Simulation results showed that the optimum frequency range lies in 200-800MHz.

The path gain variation is observed for both free space and body and effects associated with near field and far field are studied.

FUTURE WORK

The design for targeted drug delivery system can be modified so that multiple patients can be handled by a single transmitter controlled by a care taker or nurse. If there is a provision for two-way transmission (transmission from transmitter to receiver and from receiver to transmitter), then it increases the feasibility of the system.

ACKNOWLEDGEMENT

We would like to express our immense gratitude to our beloved chancellor Shri (Dr) Mata Amritanandamayi Devi for providing a very good motivation and inspiration for doing our research work.

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