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Universiti Malaysia PAHANG

Early breast cancer detection using patient symptomatic breast images by Finite Element Analysis aided by COMSOL

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BACKGROUND OF STUDY

- most common cancer
- Chemotherapy
- transdermal technology

MOTIVATION

- transdermal application has limitation
- drugs must obviously be able to penetrate skin
- suitable modification

OBJECTIVES

- To convert Materilaise's Interactive Medical Image Control System (MIMICS) image files into COMSOL
- To determine the drug concentration at breast tumor
- To investigate the relationship between drug diffusivity and drug delivery efficiency, and
- To evaluate the efficiency of drug delivery under other parameters (i.e. deepness of tumor, temporal and spatial placement of transdermal patch).

RESEARCH SCOPE

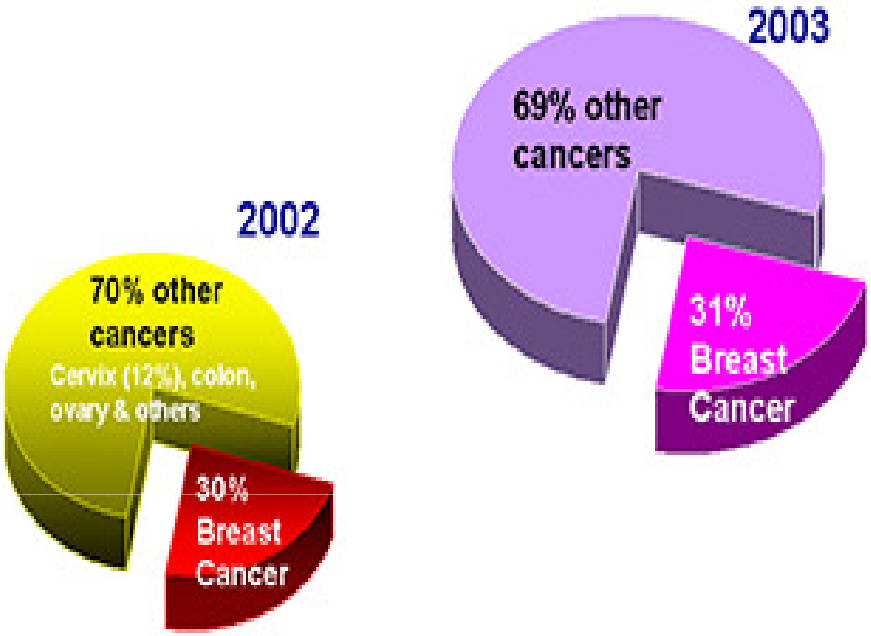
- efficiency of drug delivery

LITERATURE REVIEW

OVERWIEW OF BREAST CANCER STATISTIC

Breast cancer in University Malaya Medical Centre, Kuala Lumpur 1993-2003, with total number of 1818 cases.

Source: College Of Radiology Breast Health Information Centre (2008)



Percentage of different kinds of cancer in Malaysian women, in the year of 2002 and 2003

Source: College Of Radiology Breast Health Information Centre (2008)

	1994	1995	1998
Breast	260	320	339
Lung	244	254	272
Cervix	165	142	177
Colorectal	128	164	149
Leukemia	128	142	139
Stomach	99	105	103
Liver	98	102	106
Ovary	88	95	122

Deaths from cancers in Malaysia women for the years of 1994, 1995 and 1998

Source: Vital Statistic Malaysia

CONVENTIONAL BREAST CANCER DRUG THERAPY

- Chemotherapy

-killing microorganisms or cancerous cells

-have no the capability to distinguish between the cancer cells and normal cells

-side effects

DRUGS

- DOCETAXEL

-stopping the cancer cells from separating into two new cells (Cancer Health UK, 2009)

- DOXORUBICIN (ADRIAMYCIN)

-Doxorubicin works by binding to the cancer cells' DNA and blocking an important enzyme called topo-isomerase II (Cancer Health UK, 2009)

- HERCEPTIN (TRASTUZUMAB)

-stop cancer cell growth

- PACLITAXEL (TAXOL)

-slows or stops the growth of cancer cells in body

- METHOREXATE (MAXTREX)

-stops some cells working properly (Cancer Health UK, 2009)

SOFTWARE

- MATERILAISE'S INTERACTIVE MEDICAL IMAGE CONTROL SYSTEM (MIMICS)
- COMSOL

TRANSDERMAL APPLICATION

- alternative route (Stanley, S., 2004)
- side effects could be eliminated
- reduced pharmacological dosing (Girish, C., 2006)
- controlled release of drugs (Department of Pharmacology, University of Dublin)

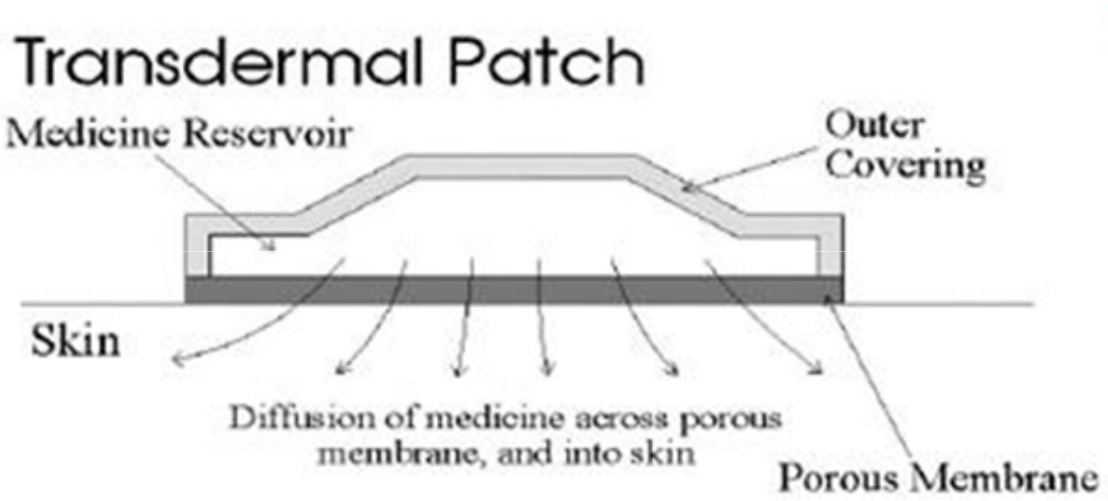
PATCH DESIGN

Components of transdermal patch, which consisted of five main key elements such as liner, drug, adhesive, membrane and backing

Source: Shreeraj, S. (2008)

- Release of the medicament from the vehicle
- Penetration through the skin barrier
- Uptake of the drug by the capillary network in the dermal papillary layer
- Activation of the pharmacological response. (Girish, C., 2006)

PENETRATION OF DRUG



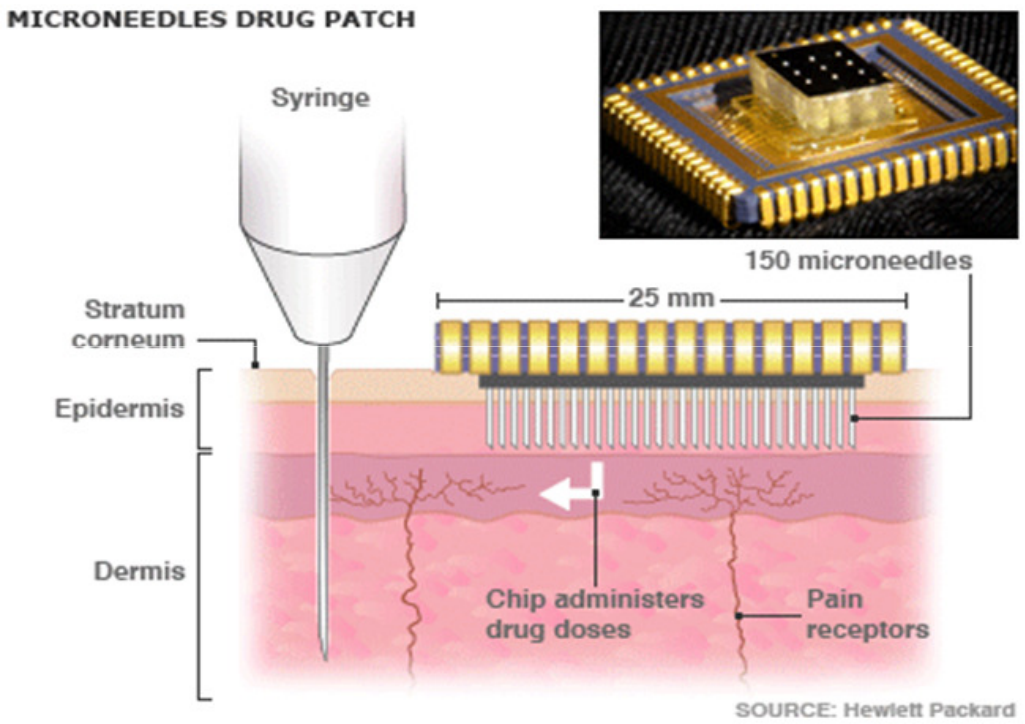
Mechanism of action of transdermal patch, diffusion

Source: Shreeraj, S. (2008)

FICK'S LAW

- Fick's Law of Diffusion
- $\partial c/\partial t = D [(1/r) (\partial/\partial r) (r \partial c/\partial r) + \partial^2 c/\partial z^2]$
- Where c is the concentration of the drug and D is its diffusivity. (Datta, A. and Rakesh, V., 1996)

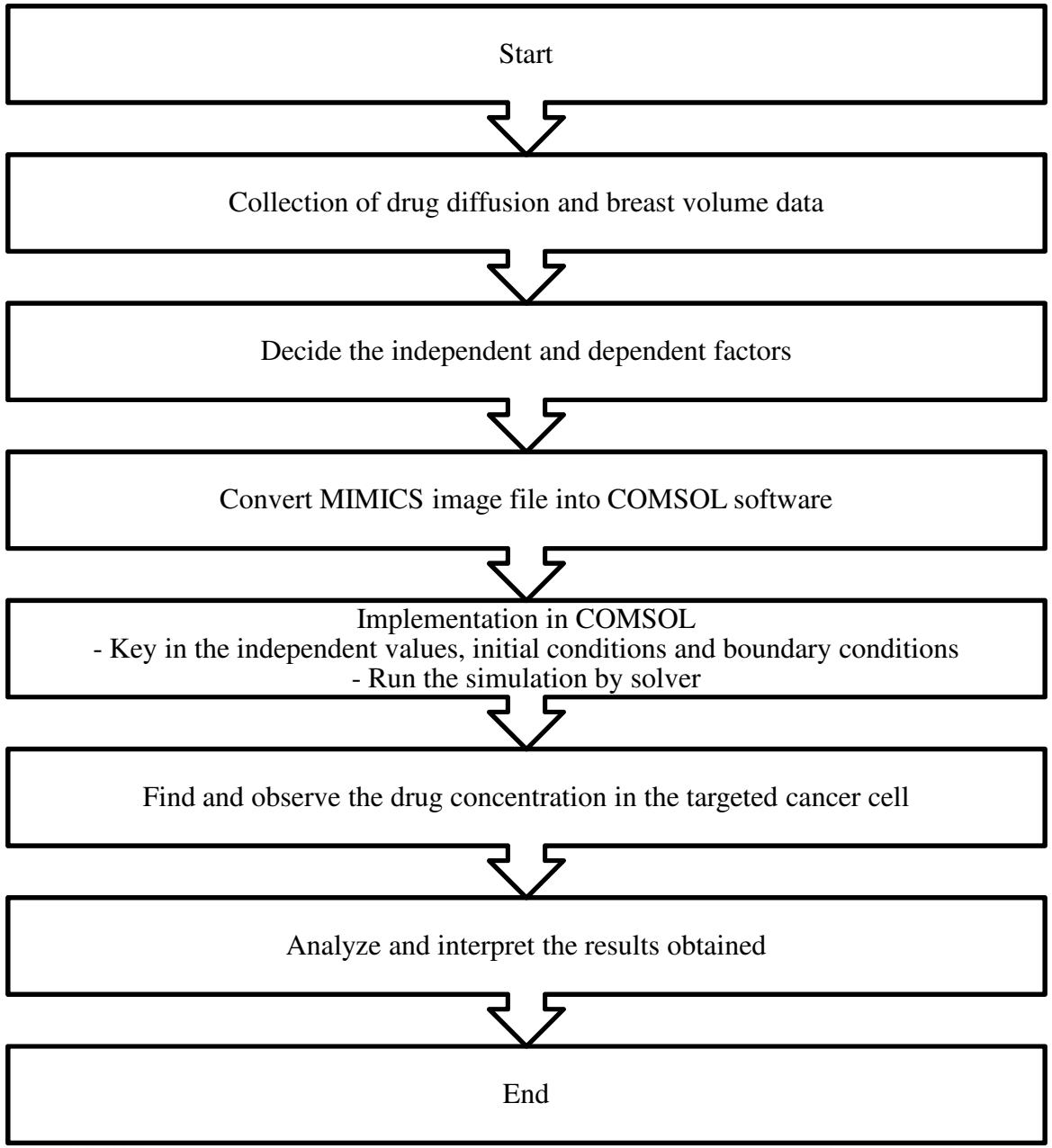
ENHANCEMENT TECHNIQUES



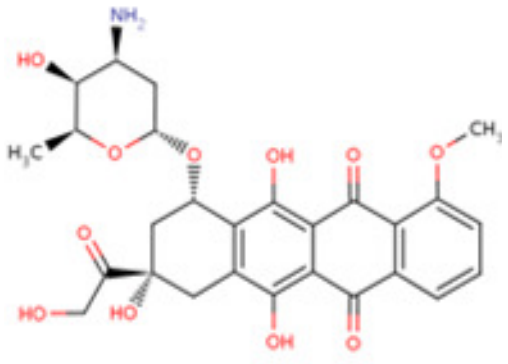
Microneedles drug patch

Source: Packard, H. (2007)

METHODOLOGY


Start
Collection of drug diffusion and breast volume data
Decide the independent and dependent factors
Convert MIMICS image file into COMSOL software
Implementation in COMSOL
- Key in the independent values, initial conditions and boundary conditions
- Run the simulation by solver
Find and observe the drug concentration in the targeted cancer cell
Analyze and interpret the results obtained
End

COLLECTION OF DRUG DIFFUSIVITY DATA

Property	Value
Standard diffusivity	2.7×10^{-10} cm^2/s (Kaowumpai, W. et. al., 2008)
Average Molecular Weight	543.5193
Chemical Formula	$C_{27}H_{29}NO_{11}$
Chemical Structure	

COLLECTION OF BREAST VOLUME DATA

- The method employed for breast volume calculation from the mammograms was that used by Katariya and colleagues and Hoe and colleagues, which is highly reproducible
- $\frac{1}{3}\pi r^2 h$ (Senie, R. et. al., 1980)

-where r was half the breast width and h the breast height

IMPLEMENTATION IN COMSOL

- STEPS FOR SOLVING SPECIFIED PROBLEM IN COMSOL

-Convert the MIMICS image file to COMSOL raw file (.mph)

-Defining material properties and initial conditions

-Defining boundary conditions

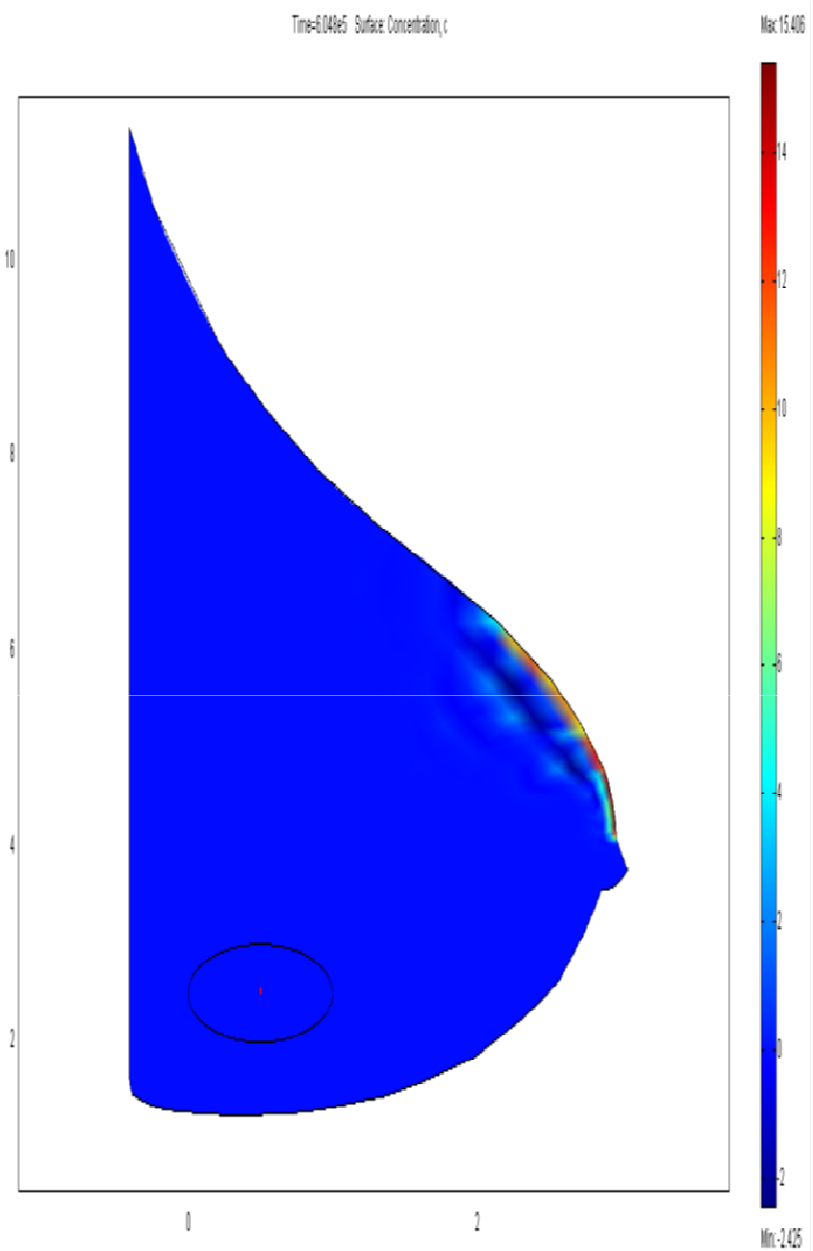
-Specify solver parameters

-Postprocessing

EFFICIENCY OF DRUG DILIVERY UNDER DRUG DIFFUSIVITY PARAMETER

Drug Diffusivity, D (cm^2/s)	Drug Concentration, c (mol/cm^2)
2.7×10^{-9}	1.004595×10^{-13}
2.7×10^{-8}	3.178387×10^{-14}
2.7×10^{-7}	4.417303×10^{-8}
2.7×10^{-6}	0.006829
2.7×10^{-5}	0.00932
2.7×10^{-4}	0.001227
2.7×10^{-3}	1.227515×10^{-4}
2.7×10^{-2}	1.227515×10^{-5}
2.7×10^{-1}	1.227515×10^{-5}

Concentration of drug at breast tumor with different drug diffusivity, from 10-9 to 10-1



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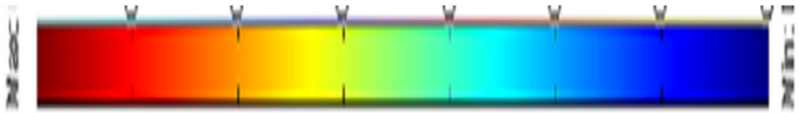
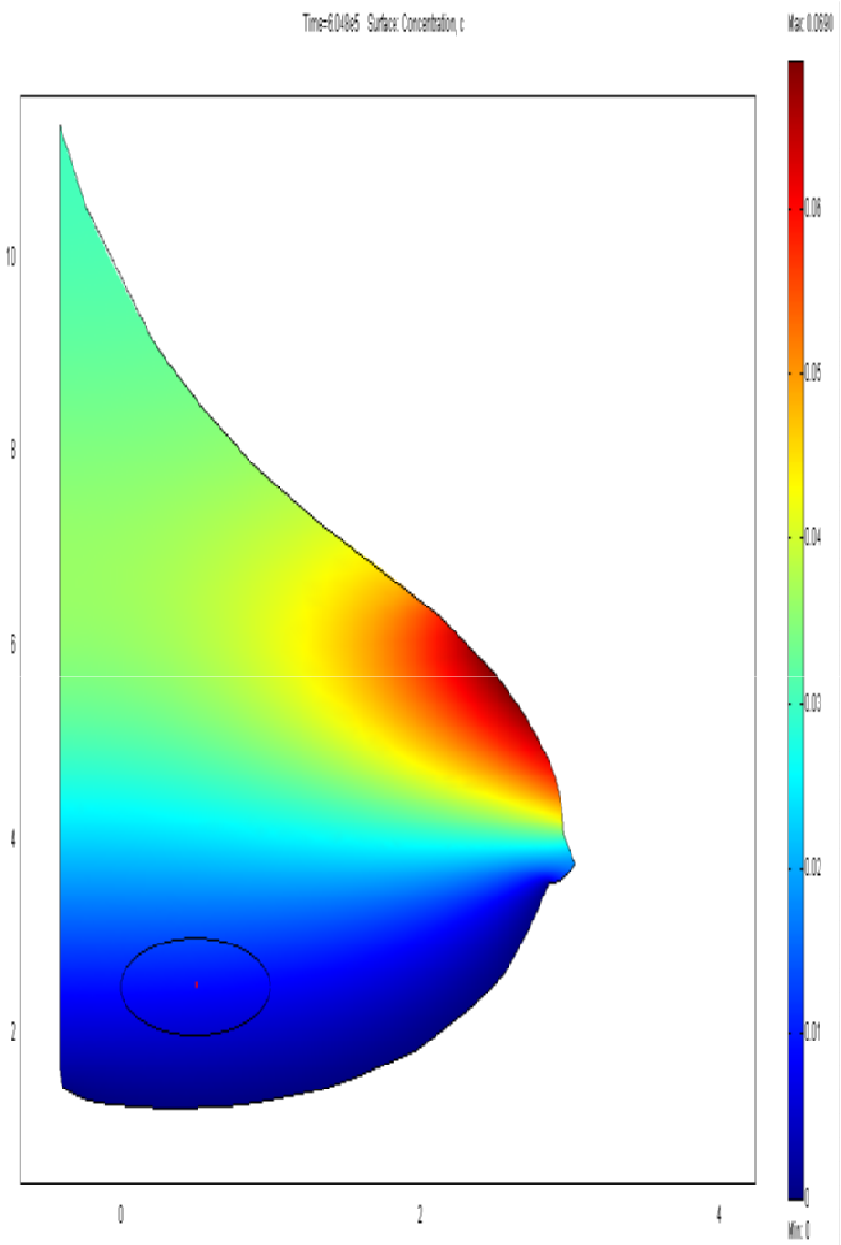
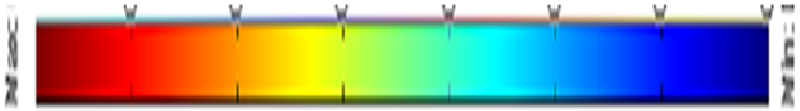
Drug's concentration after one week using drug diffusivity of 2.7×10^{-9} cm^2/s



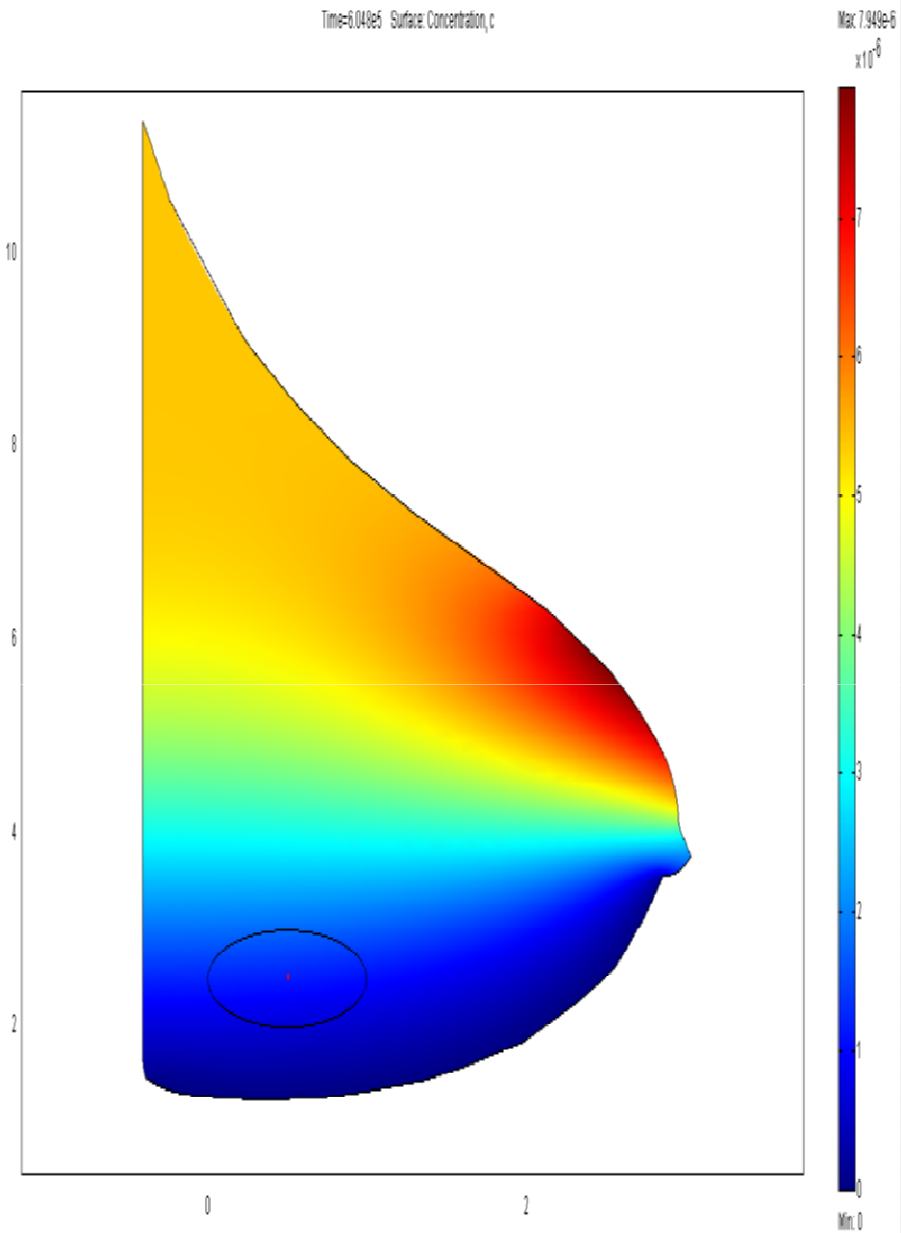
Indication of colours, from maximum to minimum



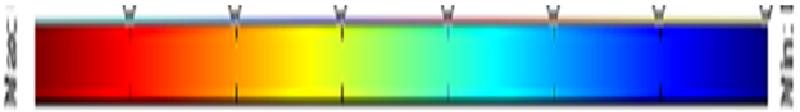
Drug's concentration after one week using drug diffusivity of 2.7×10^{-5} cm^2/s



Indication of colours, from maximum to minimum



Drug's concentration after one week using drug diffusivity of 2.7×10^{-1} cm^2/s



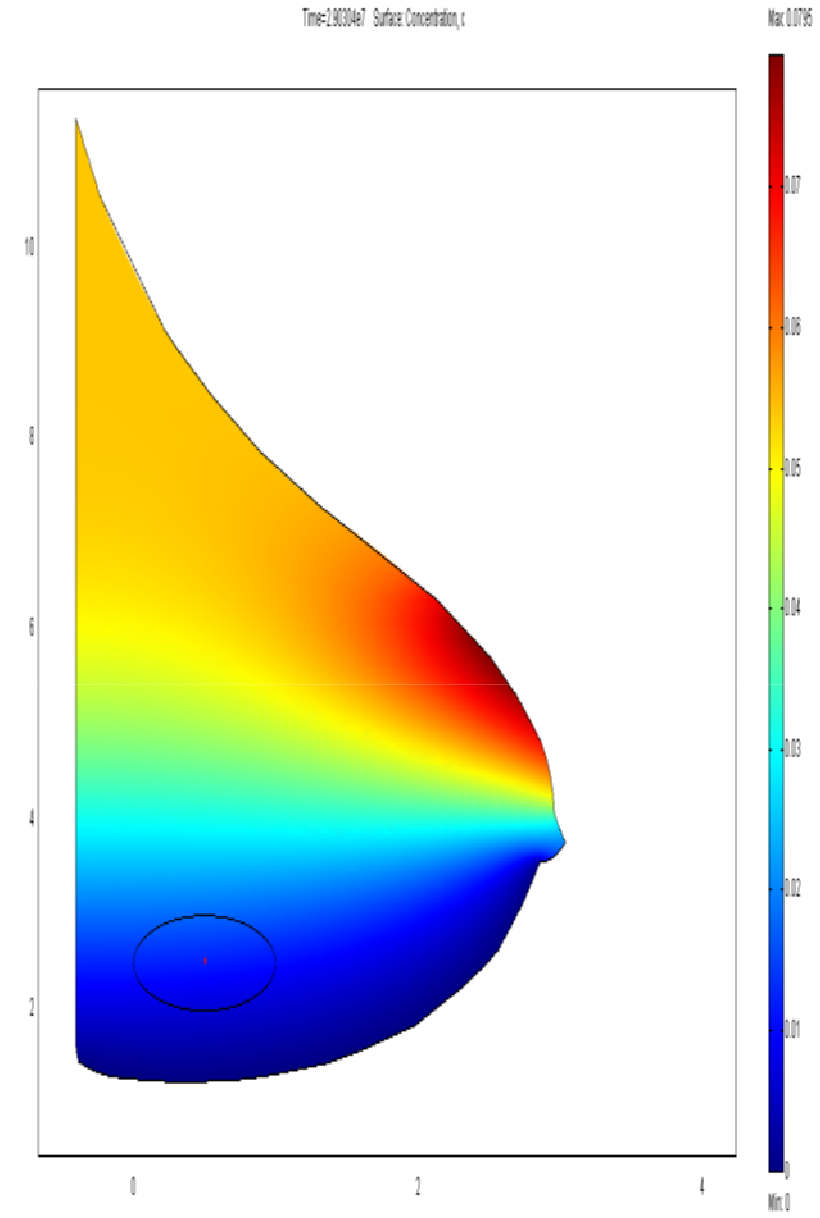
Indication of colours, from maximum to minimum

- Highest drug concentration was found at diffusivity of 2.7×10^{-5} cm^2/s
- Balance between diffusion and drug release rate from the reservoir system
- Increase in length of the diffusional pathway

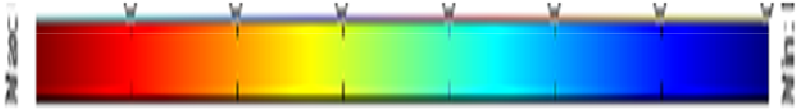
EFFICIENCY OF DRUG DELIVERY UNDER DEEPNESS OF BREAST TUMOR PARAMETER

Deepness of Breast Tumor	Drug Concentration, c (mol/cm^3)
Top of the breast	0.012219
Bottom of the breast	0.056516

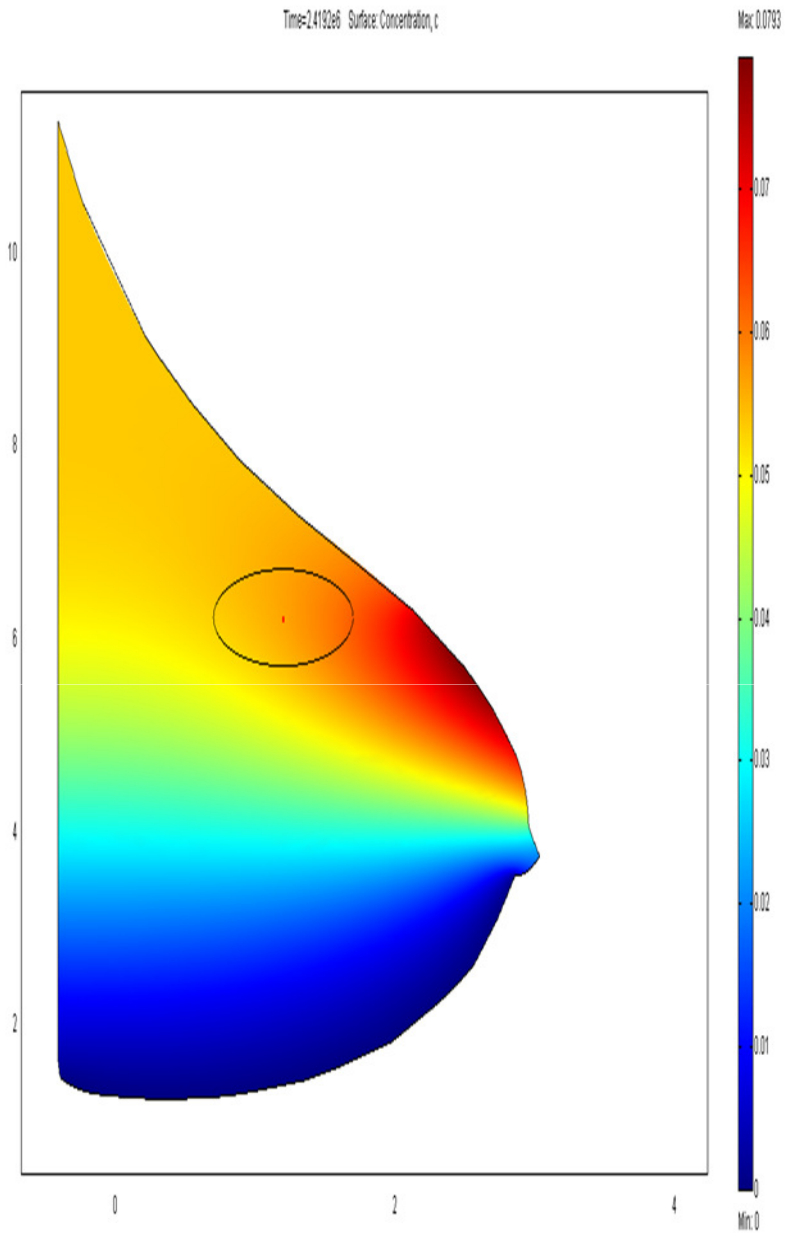
Concentration of drug at tumor that grown at the top and bottom of breast



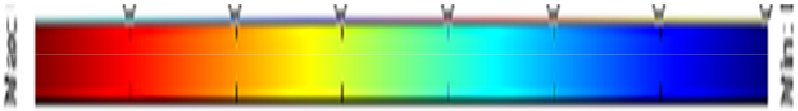
Diffusion of drug into skin to reach target site, tumor at the bottom of breast after one month



Indication of colours, from maximum to minimum



Diffusion of drug into skin to reach target site, tumor at the top of breast after one month



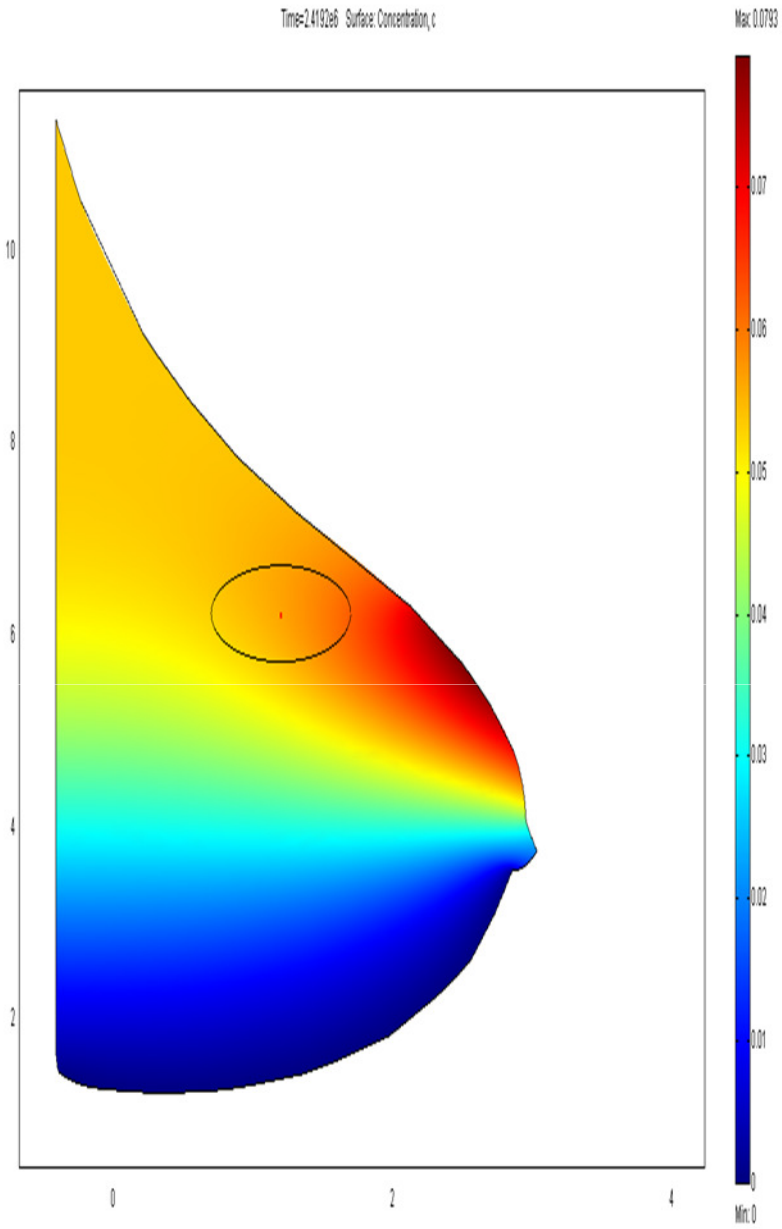
Indication of colours, from maximum to minimum

- drug distribution had high concentration around the corner of patch and stratum corneum
- interphase drug concentrations have a direct connection with the diffusion path

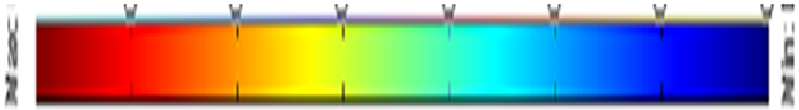
EFFICIENCY OF DRUG DELIVERY UNDER SPATIAL PLACEMENT OF TRANSDERMAL PATCH

Spatial Placement	Drug Concentration, c (mol/cm^3)
Top of the breast	0.012219
Bottom of the breast	0.061773

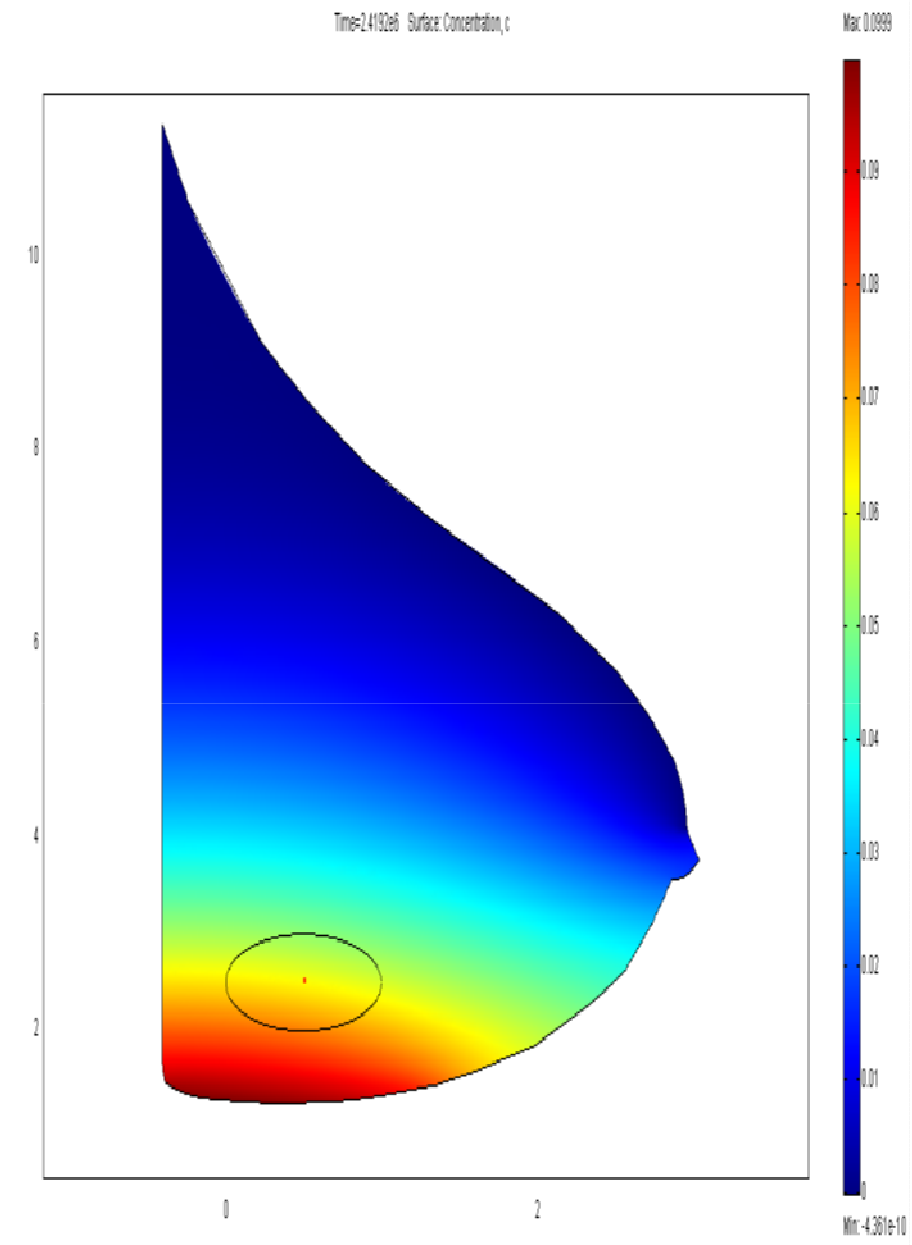
Concentration of drug at tumor when patch applied at different locations



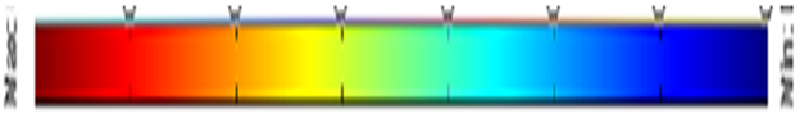
Diffusion of drug into skin to reach target site, tumor at the top of breast after one month



Indication of colours, from maximum to minimum



Diffusion of drug into skin to reach tumor after one month when patch was applied at the bottom of breast



Indication of colours, from maximum to minimum

- deeper the breast tumor was grown would cause lesser drug concentration being diffused and reached on tumor was discovered
- applying the transdermal patch on different location due to the nearer of patch to the tumor, the drug concentration able to diffuse to the tumor will be higher

CONCLUSION AND RECOMMENDATIONS

CONCLUSION

- optimal drug's concentration at the drug diffusivity of 10^{-5}. Below or above this optimal drug diffusivity, the drug delivery efficiency would be affected
- indirect relationship between deepness of breast tumor and spatial placement of transdermal patch

RECOMMENDATIONS

- In this study, only diffusion condition was considered. However, there is still convective condition occurs between the transdermal patch and skin. Therefore, in future work, this model can be improved by accommodating the convective condition.

- The present simulation was carried out by using finite element modeling (FEM) with two-dimensional geometry. This model may be improved by constructing a more complex geometry

- Highest drug's concentration is not always good to patient

-For instance, a recommended dose of doxorubicin was 50mg/m^2. (Kaoumpai, W. et. al., 2008)

Q & A