SINGLE-SIDED MAGNETIC NANOPARTICLES IMAGING SCANNER FOR EARLY DETECTION OF BREAST CANCER

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Dedicated to my late parents Alhaji Abdulkadir Adamu and Hajiya Zainab Abdulkadir

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ABSTRACT

Electromagnetic coils form the basis of magnetic particle imaging (MPI) scanners. Previous scanner designs employ Helmholtz coil arrangement which has low sensitivity and high cost of fabrication. Furthermore, the scanners have long signal acquisition time and high memory requirement. This research focuses on developing a simple, low-cost and low memory demanding one-dimensional MPI scanner capable of imaging the position and concentration of magnetic nanoparticles (MNPs), using electromagnetic coils in the form of solenoids. The scanner produces an oscillatory magnetic field to excite the MNPs and a static magnetic field to confine the region of interest. The MNPs reacted with a nonlinear magnetisation response, inducing a voltage signal that was measured with an appropriate gradiometer pickup coil. In Fourier space, the received voltage signal consists of the fundamental excitation frequency and harmonics. This research utilises the second harmonic response of the MNPs to determine their position and concentration. Analogue Bandpass and Bandstop filters were designed for signal excitation and reception. Resovist and Perimag MNPs in liquid and immobilised form were used as tracer materials, which were moved to different spatial positions through the field of view (FOV), to record the induced voltages. The magnitude response of the Bandpass filter with 22.8 kHz fundamental frequency shows a flat amplitude in the passband with a smooth roll-off rate of ±80 dB/pole, while the Bandstop filter efficiently attenuates the fundamental frequency and passed the 45.6 kHz second harmonic frequency. Results of the excitation coil design revealed that a magnetic field within the range of 0.8 mT to 4.4 mT was obtained, while a voltage in microvolts range was induced in the gradiometer pickup coil. The contour maps derived from imaging one and two samples of the MNPs in the *XY*-plane revealed their position and shape. Additionally, the average threshold of the peak signal amplitude was obtained as 10.63 µV that would indicate the presence of MNPs concentration sufficient for cancer detection. The developed single-sided MPI scanner has a spatial resolution of less than 1 mm, a pixel resolution of 51.5 megapixels and 42.1 ms image acquisition time. Thus, the outcome of this research showed that the developed single-side MPI scanner has a potential in the detection of MNPs, which could help in sentinel lymph node biopsy for breast cancer diagnosis.

ABSTRAK

Gegelung elektromagnet membentuk asas pengimbas zarah magnet (MPI). Rekaan pengimbas sebelumnya menggunakan pengaturan gegelung Helmholtz yang mempunyai kepekaan yang rendah dan kos fabrikasi yang tinggi. Selain itu, pengimbas mempunyai masa ambilan isyarat yang lama dan memerlukan *memory* yang tinggi. Kajian ini tertumpu kepada pembangunan pengimbas MPI yang ringkas, berkadar rendah dan pengunaan *memory* yang rendah dalam satu dimensi yang mampu mengimbas kedudukan dan kepekatan nanopartikel magnetik (MNPs), dengan menggunakan gegelung elektromagnet dalam bentuk solenoid. Pengimbas menghasilkan medan magnet *oscillatory* bagi mengalakkan MNPs dan medan magnet statik untuk menghadkan kawasan tertumpu. MNP memberi tindak balas kepada *nonlinear magnetisation*, dan menghasilkan isyarat voltan yang diukur dengan gegelung pikap *gradiometer* yang bersesuaian. Di dalam ruang Fourier, isyarat voltan yang diterima terdiri daripada asas frekuensi pengujaan dan harmonik. Kajian ini menggunakan tindak balas harmonik kedua MNP untuk menentukan kedudukan dan kepekatan MNP. Penapisan *Bandpass* dan *Bandstop* Analog telah direka bagi pengujaan dan penerimaan isyarat. MNP *Resovist* dan *Perimag* dalam bentuk cecair dan *immobilized* telah digunakan sebagai bahan pengesan, yang dialihkan ke kedudukan spasial yang berlainan melalui bidang pandangan atau dikenali sebagai *Field of View* (FOV), bagi mencatat voltan teraruh. Tindak balas magnitud penapis *Bandpass* dengan frekuensi asas 22.8 kHz menunjukkan amplitud rata di passband dengan kadar *roll-off* pada ± 80 dB / pole, manakala penapis *Bandstop* cekap mengatasi frekuensi asas dengan 45.6 kHz dan melepasi frekuensi harmonik kedua. Keputusan menunjukkan reka bentuk pengujaan gegelung medan magnet didalam julat antara 0.8 mT hingga 4.4 mT telah diperoleh, manakala pelbagai nilai voltan dalam mikrovolt diinduksi ke dalam gegelung pikap *gradiometer*. Peta kontur yang diperolehi daripada pengimejan satu dan dua sampel MNP dalam *XY-plane* menunjukkan kedudukan dan bentuknya. Di samping itu, maksima purata isyarat puncak amplitud diperolehi adalah 10.63 μV yang akan menunjukkan kehadiran

kepekatan MNP yang memadai untuk mengesan sel kanser. Pengimbas MPI satu dimensi yang dimajukan mempunyai resolusi spatial kurang dari 1 mm, resolusi piksel 51.5 megapixel dan masa pemerolehan imej 42.1 ms. Oleh itu, hasil kajian ini menunjukkan bahawa pengimbas MPI satu dimensi yang dimajukan mempunyai potensi untuk mengesan MNPs, yang boleh membantu dalam biopsi nodus limfa sentinen untuk diagnosis kanser payudara.

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LIST OF SYMBOLS AND ABBREVIATIONS

A_D	-	Drive field amplitude
B_s	-	Magnetic flux density
F_e	-	Ferrum
H_0	-	Amplitude of excitation frequency
H_D	-	Drive magnetic field
H_S	-	Selection magnetic field
H_{ac}	-	Alternating current magnetic field
H_{dc}	-	Direct current magnetic field
M_s	-	Saturation magnetisation
T_m	-	Total acquisition time
V_0	-	Known volume
V_h	-	Hydrodynamic volume
V_m	-	Magnetic core volume
V_{pp}	-	Voltage peak-to-peak
X_C	-	Capacitive reactance
X_L	-	Inductive reactance
c_0, c	-	Nanoparticles concentration
f_0	-	Fundamental frequency
f_D	-	Drive field frequency
f_c	-	Centre frequency
f_r	-	Resonant frequency
f_s	-	Selection field frequency
k_B	-	Boltzmann constant
m_s	-	Magnetic moment at saturation
$\bar{\mu}$	-	Mean magnetic moment
μ_0	-	Permeability of vacuum

τ_0 - Time constant

τ_B - Brownian relaxation

τ_N - Neel relaxation

τ_{eff} - Effective relaxation

℃ - Degree Celsius

h - Sensitivity profile of magnetic field

A - Amperes

A/m - Ampere per meter

BW - Bandwidth

C - Capacitance

D - Nanoparticle diameter

G - Gradient matrix

GHz - Giga hertz

H - Magnetic field strength

I - Current

K - Anisotropy energy

L - Inductance

M - Magnetisation

N - Number of turns

P - Coil sensitivity

Q - Quality factor

R - Resistance

RC - Resistance-capacitance

S - System Matrix

T - Absolute temperature

V - Voltage

W - Weighting matrix

X - Reactance

Z - Impedance

dB - Decibel

$k\Omega$ - Kilo ohms

kHz - Kilo hertz

mV - Millivolt

mg - Milligram
r - Spatial point
t - Time
u - Recorded signal
ζ - Damping factor
η - Dynamic viscosity
λ - Regularization parameter
μl - Microliter
ξ - Langevin parameter
ω - Angular frequency
1D - One-dimensional
2D - Two-dimensional
3D - Three-dimensional
AC - Alternating current
ACS - Alternating current susceptibility
ART - Algebraic reconstruction technique
AWG - American wire gauge
BPF - Bandpass filter
BSF - Bandstop filter
CAD - Computer-aided design
CAD - Coronary artery disease
CT - Computed tomography
DAC - Digital-to-analogue converter
DAQ - Data acquisition
DC - Direct current
DDS - Direct digital synthesis
DNA - Deoxyribonucleic acid
EC - Excitation coil
FC-PC - field cancellation pickup coil
FFL - Field free line
FFP - Field free point
FFR - field free region
FOV - Field of view

GB - Gigabyte
HDD - Hard drive
HPF - Highpass filter
IDC - Inductive ductal carcinoma
LabVIEW - Laboratory virtual instrument engineering workbench
LPF - Lowpass filter
MATLAB - Matrix laboratory
MNPs - Magnetic nanoparticles
MPI - Magnetic particle imaging
MPS - Magnetic particle spectrometer
MRA - Magnetic resonance angiography
MRI - Magnetic resonance imaging
MRX - Magnetic relaxation
NI - National instruments
PBR - Projection-based reconstruction
PC - Personal computer
PET - Positron emission tomography
PLA - Polylactic acid
RAM - Random access memory
RBCs - Red blood cells
RF - Radio frequency
RFID - Radio frequency identification
RLC - Resistor-inductor-capacitor
rms - Root mean square
RNA - Ribonucleic acid
SFC - Selection field coil
SLN - Sentinel lymph node
SLNB - Sentinel lymph node biopsy
SNR - Signal-to-noise ratio
SPECT - Single photon emission computed tomography
SPIO - Superparamagnetic iron-oxide
SPIONs - Superparamagnetic iron-oxide nanoparticles
SQUID - Superconducting quantum interference device

SVD	- Singular value decomposition
TB	- Terabyte
THD	- Total harmonic distortion
USB	- Universal serial bus
VHF	- Very high frequency
VLF	- Very low frequency
w/w	- Weight per weight

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CHAPTER 1

INTRODUCTION

1.1 Research background

Magnetic particle imaging (MPI) is an innovative imaging modality that carries out a direct measurement of the magnetisation of ferromagnetic nanoparticles to quantify their local concentration. Superparamagnetic iron-oxide nanoparticles (SPIONs) are usually employed as tracer substance in MPI, due to their tiny size and exhibition of superparamagnetism. These SPIONs are injected into a target area, then excited by an external magnetic field (drive field) and the response of the particles is recorded, which is proportional to the concentration of the SPIONs (Gleich 2013, Saritas *et al*., 2013 & Sadiq *et al*., 2015).

MPI technique was invented in 2001 by Bernhard Gleich and Jürgen Weizenecker, who first reported about the concept in 2005. MPI offers a unique combination of features that sets it apart from other conventional methods for medical imaging. An essential theory for describing the magnetic behaviour of superparamagnetic particles is the Langevin theory, which is evident from the assumption that the particles are always in thermal equilibrium (Gleich & Weizenecker, 2005).

The spatial distribution of magnetic nanoparticles (MNPs) used as tracer material can be determined by measuring the change in magnetisation of the tracer material in a time-varying magnetic field. Figure 1.1 demonstrates the particle magnetisation, showing the relationship between the external magnetic field applied

to the MNPs and their magnetisation response. The nonlinearity of the MNPs response is depicted by the green curve in Figure 1.1. *M* is the magnetisation of the magnetic nanoparticles while *H* is the applied excitation magnetic field with peak-to-peak amplitude of *A* to *-A*.

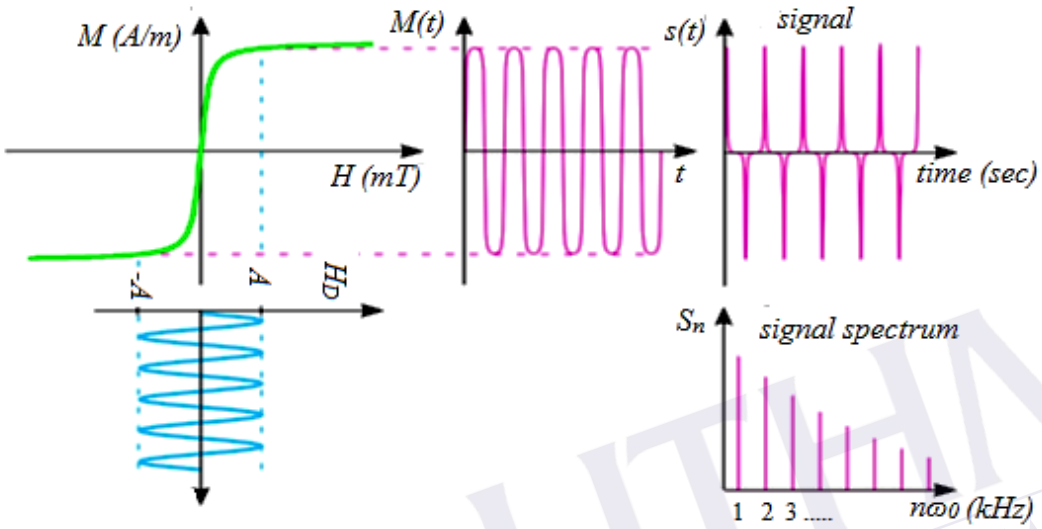

Figure 1.1: Particle Magnetisation (Borget *et al.*, 2012)

The dynamic region of the magnetisation curve is nonlinear when a periodic signal of -A to A is applied, while the saturation region started when the area used is above A. No further magnetisation is produced at saturation, and this results in the presence of harmonics in the established signal. The magnetization response *M(t)* with respect to time is shown next in Figure 1.1, while the corresponding voltage signal *s(t)* in time domain is shown after that. The harmonics from the magnetisation of the particles are obtained by conducting a fast fourier transform on *s(t)* to reveal the harmonic spectrum, S_n as shown in the last plot of Figure 1.1. The amplitude of the voltage signals recorded at these harmonics are used to reconstruct tomographic images that will indicate the existence of the magnetic tracer material. To spatially and temporally decide a spreading of SPIONs tracer within a patient, the communication between static and dynamic magnetic fields and the typical magnetisation behaviour of the tracer material is exploited.

The dynamic magnetic field (also known as the excitation field) is generated by an excitation coil with an AC signal source. The static magnetic field on the other hand is generated by a gradient coil (selection field coil) with a DC signal source. The

excitation magnetic field is superimposed on the selection magnetic field to create the field-free region, where only the magnetic nanoparticles contribute to the recorded signal.

MPI offers some advantages over other medical imaging methods, which could make it a suitable technique for clinical examinations (Knopp & Buzug 2012, Gräfe *et al*., 2012). The first advantage of MPI is the quantitative measurement. The measured MPI signal is directly proportional to the concentration of the tracer material (follows a system of linear equations). That is, the higher the concentration, the stronger the signal received and vice versa. This means that no signal will be recorded when there is no tracer material present in the target area. The concentration to signal correlation is known to exist from other methods in nuclear medicine, such as the single photon emission computed tomography (SPECT), magnetic resonance imaging (MRI) and positron emission tomography (PET).

Secondly, MPI offers high spatial and temporal resolution. This advantage can further be utilised to implement a real-time MNPs imaging. The third advantage of MPI is high sensitivity in imaging. The MPI signal is acquired directly from the tracer, not from the tissues. This feature makes the sensitivity of MPI much superior to that of MRI. Additionally, MPI offers flexibility in the selection of acquisition parameters, to achieve a particular sensitivity or resolution.

Fourthly, there is no ionisation radiation in MPI. The magnetic fields used in MPI are either periodic or static, which pose no risk to patients (no adverse or long-term effects). Finally, MPI signals were reported to be acquired in less than 0.1 seconds as compared to other imaging modalities that have acquisition time of over one minute.

MPI as a medical imaging modality finds applications similar to that of the established modalities, for instance in diagnosis and treatment of diseases, and cell tracking and labelling. Moreover, MPI targets applications demanding fast, dynamic imaging, such as blood flow visualisation in the case of coronary artery diseases, cancer identification, for example, sentinel lymph node biopsy (SLNB) or any application where tracers are employed for diagnosis using a PET, SPECT or MRI (Gleich *et al*., 2012). In conjunction with advances in imaging technologies such as MRI, computed tomography (CT), and fluoroscopy, MPI as a novel imaging technology, however, is promising in holding excellent imaging properties of sound spatial resolution, high signal-to-noise ratio (SNR), and high sensitivity without ionising emission (Utkur *et al*., 2017).

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