A DOUBLE-BLINDED PLACEBO-CONTROLLED INVESTIGATION INTO THE EFFECT OF THERAPEUTIC ULTRASOUND ON RADIAL ARTERY BLOOD FLOW

By

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Dissertation submitted in partial compliance with the requirements for the Master's Degree in Technology: Chiropractic

Durban University of Technology

I, Desiree Varatharajullu, do hereby declare that this dissertation is representative of my own work in both conception and execution (except where acknowledgements indicate to the contrary)

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Desiree Varatharajullu

Approved for Final Submission

______________________________________ Date: ___________________________
Dr. J. Shaik
DEDICATION

I dedicate this dissertation to:

God, for the support, guidance and protection He has bestowed upon me through all the hard times and for His Helping Hand during all the good times

My Mum, Moganayagie, thank you is not enough for all the sacrifices you made to ensure that I achieve success. Your strength and guidance has made me into the woman I am today

My Dad, Moonsamy, thank you for giving me the opportunity in pursuing my career in Chiropractic and for all your encouragement throughout the years

My brothers’ Kershen and Jason for putting up with my “tantrums” and always supporting me through good and bad times

My wonderful grandparents, for your unfailing love and support especially when I needed it the most. I love you both dearly

My best friend, Pavendren Govender, you have been my rock through some pretty tough times and I can’t thank you enough
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ABSTRACT

Aim: To investigate the effect of therapeutic and sham ultrasound on radial artery blood flow (m.s\(^{-1}\)) and radial arterial lumen diameter (mm).

Subjects: Fifty healthy asymptomatic volunteers between the ages of 18-38 years.

Methodology: The subjects were randomly allocated into one of five intervention groups (A-E). Group A received continuous ultrasound at 0.2 W.cm\(^{-2}\) for 5 minutes, Group B received pulse ultrasound at 0.2 W.cm\(^{-2}\) for 5 minutes, Group C received continuous ultrasound at 1.5 W.cm\(^{-2}\) for 5 minutes, Group D received pulse ultrasound at 1.5 W.cm\(^{-2}\) for 5 minutes and Group E received sham ultrasound at 0 W.cm\(^{-2}\) for 5 minutes. Baseline radial artery blood flow (m.s\(^{-1}\)) and radial artery lumen diameter (mm) readings were taken prior to the commencement of the therapeutic or sham ultrasound application using a Doppler ultrasound. At four minutes of application (during the therapeutic or sham ultrasound application), another set of blood flow and arterial lumen diameter measurements were taken. The final blood flow and arterial lumen diameter measurements were taken one minute after the therapeutic or sham ultrasound application was stopped.

Results: The mean (± SD) radial artery blood flow and radial artery lumen diameter at baseline was 0.197 (± 0.060) m.s\(^{-1}\) and 2.4 (± 0.6) mm respectively. In Group A, the mean (± SD) radial artery blood flow during ultrasound application and one-minute after ultrasound application was 0.193 (± 0.070) m.s\(^{-1}\) and 0.179 (± 0.073) m.s\(^{-1}\) respectively. The mean (± SD) radial artery lumen diameter in Group A at the two time intervals was 2.2 (± 0.5) mm and 2.2 (± 0.3) mm respectively. In Group B, the mean (± SD) radial artery blood flow during ultrasound application and one-minute after ultrasound application was 0.187 (± 0.067) m.s\(^{-1}\) and 0.195 (± 0.041) m.s\(^{-1}\) respectively. The mean (± SD) radial artery lumen diameter in Group B at the two time intervals was 2.4 (± 0.4) mm and 2.3 (± 0.5) mm respectively. In Group C, the mean (± SD) radial artery blood flow during ultrasound application and one-minute after ultrasound application was 0.225 (± 0.088) m.s\(^{-1}\) and 0.186 (± 0.071) m.s\(^{-1}\) respectively. The mean (± SD) radial artery lumen diameter in Group C at the two time intervals was 2.4 (± 0.7) mm and 2.7 (± 0.8) mm respectively. In Group D, the mean (± SD) radial artery blood flow during ultrasound application and one-minute after ultrasound application was 0.215 (± 0.080) m.s\(^{-1}\) and 0.200 (± 0.081) m.s\(^{-1}\) respectively. The mean (± SD) radial artery lumen diameter in Group
D at the two time intervals was 2.4 (± 0.8) mm and 2.4 (± 0.7) mm respectively. In Group E, the mean (± SD) radial artery blood flow during ultrasound application and one-minute after ultrasound application was 0.200 (± 0.067) m.s\(^{-1}\) and 0.182 (± 0.075) m.s\(^{-1}\) respectively. The mean (± SD) radial artery lumen diameter in Group E at the two time intervals was 2.5 (± 0.7) mm and 2.3 (± 0.5) mm respectively. There was no significant change in radial artery blood flow and radial artery lumen diameter over time in any individual group or between groups (p > 0.05; repeated measures ANOVA). There was an overall weak positive correlation between radial artery blood flow and radial artery lumen diameter at baseline (r = 0.508), during (r = 0.541) and after (r = 0.532) the therapeutic or sham ultrasound application.

**Conclusion:** The results of this study showed that continuous, pulse or sham ultrasound had no significant effect on radial artery blood flow and radial artery lumen diameter. Furthermore, active ultrasound (continuous and pulse) was not superior to sham ultrasound in significantly affecting blood flow in a muscular artery.
LIST OF SYMBOLS AND ABBREVIATIONS

2-D: Two-dimensional
3-D: Three-dimensional
°C: Degrees Celsius
↑: Increase or increased
↓: Decrease or decreased
α: Alpha
β: Beta
∞: Is proportional to
ΔP: Pressure difference between the two ends of the vessel
aa: Artery
ACE: Angiotensin-converting enzyme
ANOVA: Analysis of variance
ANP: Atrial natriuretic peptide
B: Baseline
BF: Blood flow
CDC: Chiropractic Day Clinic
CO: Cardiac output
D/S: Doppler ultrasound reading during the therapeutic or sham ultrasound application
D/SA: Doppler ultrasound reading after the therapeutic or sham ultrasound application
DUT: Durban University of Technology
e.g.: Example
F: Flow
F/A: Forearm
H⁺: Hydrogen ions
HR: Heart rate
Hz: Hertz
i.e.: That is
L: Vessel length
LCD: Liquid crystal display
m.s⁻¹: Meters per second
MHz
min:
mm:
mmHg:
n:
P1:
P2:
Pts:
Q:
r:
R:
ROM:
Rx:
SMT:
SPSS:
SV:
TPs:
TPR:
TU/S:
U/S:
V:
viz.:
VOP:
W.cm\(^{-2}\)
# LIST OF TABLES

## CHAPTER TWO

<table>
<thead>
<tr>
<th>Table 2.1</th>
<th>Studies that have reported on the diameter of the radial artery</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 2.2</td>
<td>A summary of the studies which have investigated the effects of ultrasound on blood flow in animals and humans</td>
<td>21</td>
</tr>
<tr>
<td>Table 2.3</td>
<td>A summary of the recent studies that have utilised sham ultrasound as a placebo</td>
<td>25</td>
</tr>
</tbody>
</table>

## CHAPTER THREE

| Table 3.1 | The five intervention groups | 29 |

## CHAPTER FOUR

| Table 4.1 | Age, systolic and diastolic blood pressures of subjects (n = 50) who participated in the study. Data are presented as mean (± SD) | 32 |
| Table 4.2 | Intra-group and overall changes in radial artery blood flow over time | 33 |
| Table 4.3 | Intra-group and overall changes in radial artery lumen diameter over time | 34 |
| Table 4.4 | Repeated measures ANOVA for radial artery blood flow between groups | 34 |
| Table 4.5 | Repeated measures ANOVA for radial artery lumen diameter between groups | 35 |
| Table 4.6 | Pearson’s correlation between baseline radial artery blood flow and radial artery lumen diameter in all five groups | 37 |
| Table 4.7 | Pearson’s correlation between radial artery blood flow and radial artery lumen diameter during intervention in all five groups | 37 |
| Table 4.8 | Pearson’s correlation between radial artery blood flow and radial artery lumen diameter post-intervention in all five groups | 37 |
LIST OF FIGURES

CHAPTER THREE

Figure 3.1  Timeline of the experiment 30

CHAPTER FOUR

Figure 4.1  Gender percentage of the subjects (n = 50) who participated in this study 32

Figure 4.2  Pearson’s correlation between baseline radial artery blood flow and radial artery lumen diameter in all groups combined (n = 100) 35

Figure 4.3  Pearson’s correlation between radial artery blood flow and radial artery lumen diameter during the therapeutic or sham ultrasound application in all groups combined (n = 100) 36

Figure 4.4  Pearson’s correlation between radial artery blood flow and radial artery lumen diameter post-therapeutic or post-sham ultrasound application in all groups combined (n = 100) 36
LIST OF APPENDICES

Appendix A: Ethics Clearance certificate
Appendix B: Letter of Information
Appendix C: Informed Consent Form
Appendix D: Case History
Appendix E: Physical Examination
Appendix F: Data Sheet
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEDICATION</td>
<td>i</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>ii</td>
</tr>
<tr>
<td>ABSTRACT</td>
<td>iii</td>
</tr>
<tr>
<td>LIST OF SYMBOLS AND ABBREVIATIONS</td>
<td>v</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>vi</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>viii</td>
</tr>
<tr>
<td>LIST OF APPENDICES</td>
<td>ix</td>
</tr>
<tr>
<td><strong>CHAPTER ONE</strong></td>
<td>1</td>
</tr>
<tr>
<td>1.1 INTRODUCTION TO THE STUDY</td>
<td></td>
</tr>
<tr>
<td>1.2 AIMS AND OBJECTIVES OF THE STUDY</td>
<td></td>
</tr>
<tr>
<td>1.3 HYPOTHESES OF THE STUDY</td>
<td></td>
</tr>
<tr>
<td>1.4 SCOPE OF THE STUDY</td>
<td></td>
</tr>
<tr>
<td><strong>CHAPTER TWO</strong></td>
<td>4</td>
</tr>
<tr>
<td>2.1 INTRODUCTION</td>
<td></td>
</tr>
<tr>
<td>2.2 DESCRIPTION AND STRUCTURE OF ARTERIES</td>
<td></td>
</tr>
<tr>
<td>2.3 ANATOMY OF THE RADIAL ARTERY</td>
<td></td>
</tr>
<tr>
<td>2.3.1 Embryology of the Radial Artery</td>
<td></td>
</tr>
<tr>
<td>2.3.2 Origin of the Radial Artery</td>
<td></td>
</tr>
<tr>
<td>2.3.3 Course and Relations of the Radial Artery</td>
<td></td>
</tr>
<tr>
<td>2.3.4 Anomalous Variations of the Radial Artery</td>
<td></td>
</tr>
<tr>
<td>2.4 RADIAL ARTERY DIAMETER</td>
<td></td>
</tr>
<tr>
<td>2.5 FACTORS AFFECTING RADIAL ARTERY DIAMETER</td>
<td></td>
</tr>
<tr>
<td>2.6 BLOOD AND ITS CONSTITUENTS</td>
<td></td>
</tr>
<tr>
<td>2.7 CHARACTERISTICS OF BLOOD</td>
<td></td>
</tr>
<tr>
<td>2.8 BLOOD PRESSURE</td>
<td></td>
</tr>
</tbody>
</table>
2.9 BLOOD FLOW AND ITS REGULATING FACTORS

2.9.1 Mechanisms of Vasoconstriction and Vasodilation

2.10 ASSESSMENT OF BLOOD FLOW

2.10.1 Invasive Methods
2.10.2 Non-Invasive Methods

2.11 ULTRASOUND

2.12 THERAPEUTIC ULTRASOUND

2.12.1 Clinical Uses
2.12.2 Safety of Therapeutic Ultrasound
2.12.3 Biophysical Effects of Therapeutic Ultrasound
2.12.4 Blood Flow Effects of Therapeutic Ultrasound

2.13 THE HAWTHORNE AND PLACEBO EFFECTS

2.13.1 The Hawthorne Effect
2.13.2 The Placebo Effect
2.13.3 Similarities and Differences between the Hawthorne and Placebo Effects
2.13.4 Studies That Have Utilised Sham Ultrasound as a Placebo

2.14 CONCLUSION

CHAPTER THREE.........................................................................................................................................27

3.1 STUDY DESIGN
3.2 ADVERTISING
3.3 SAMPLE SIZE

3.4 INCLUSION AND EXCLUSION CRITERIA

3.4.1 Inclusion Criteria
3.4.2 Exclusion Criteria

3.5 PROCEDURE

3.5.1 Phase One
3.5.2 Phase Two

3.6 ETHICAL CONSIDERATIONS IN THIS STUDY

3.7 STATISTICAL ANALYSIS
CHAPTER FOUR  .........................................................................................................................32

4.1 DEMOGRAPHIC DATA

4.2 INTRA-GROUP ANALYSIS

4.2.1 Radial Artery Blood Flow
4.2.2 Radial Artery Lumen Diameter

4.3 INTER-GROUP ANALYSIS

4.3.1 Radial Artery Blood Flow
4.3.2 Radial Artery Lumen Diameter

4.4 CORRELATION ANALYSIS

4.4.1 Baseline
4.4.2 During the Therapeutic or Sham Ultrasound Application
4.4.3 Post-Therapeutic or Post-Sham Ultrasound Application
4.4.4 Pearson’s Correlation between Baseline Radial Artery Blood Flow and Radial Artery Lumen Diameter in All Five Groups
4.4.5 Pearson’s Correlation between Radial Artery Blood Flow and Radial Artery Lumen Diameter during Intervention in All Five Groups
4.4.6 Pearson’s Correlation between Radial Artery Blood Flow and Radial Artery Lumen Diameter Post-Intervention in All Five Groups

CHAPTER FIVE .........................................................................................................................38

5.1 DEMOGRAPHIC DATA

5.2 RADIAL ARTERY BLOOD FLOW AND RADIAL ARTERY LUMEN DIAMETER

CHAPTER SIX ..........................................................................................................................42

6.1 CONCLUSION

6.2 RECOMMENDATION

REFERENCES .............................................................................................................................43

APPENDICES
CHAPTER ONE

INTRODUCTION

1.1 INTRODUCTION TO THE STUDY
Therapeutic ultrasound has been used as a non-invasive modality in the treatment of several musculoskeletal complaints by physiotherapists (McDiarmid and Burns, 1987; Dyson, 1989; Ter Haar, 1999) and chiropractors (Nussbaum, 1997; Daniel and Rupert, 2003). Despite the wide use of therapeutic ultrasound for various musculoskeletal conditions, its effectiveness remains to be verified (Robertson and Baker, 2001). The biological effects of ultrasound can be described as either thermal (associated with continuous therapeutic ultrasound) or non-thermal (associated with pulse therapeutic ultrasound) effects (Dyson, 1987; Kitchen and Partridge, 1990; Ter Haar, 1999). It is speculated that changes in blood flow may be related to the thermal (thermogenic) effects rather than the non-thermal effects, but Ter Haar (1988) has reported that it is not possible to separate the two effects. It is, therefore, possible that pulse ultrasound could also have an effect on blood flow. Several studies have investigated the effect of therapeutic ultrasound on blood flow and have reported dissimilar results (Rubin et al., 1990; Robinson and Buono, 1995; Ware et al., 2001; Noble et al., 2007). According to Noble et al. (2007) “there remains a lack of experimental investigations examining the physiologic effects of ultrasound and how these effects may be influenced by the method of application (i.e. pulse or continuous).” This study determined the effect of continuous and pulse therapeutic and sham ultrasound on radial artery blood flow and radial artery lumen diameter using Doppler ultrasound.

1.2 AIMS AND OBJECTIVES OF THE STUDY
The primary aims of the study were:

- To determine the effect of therapeutic or sham ultrasound on radial artery blood flow (m.s⁻¹)
- To determine the effect of therapeutic or sham ultrasound on radial artery lumen diameter (mm)

The specific objectives, which included both intra- and inter-group analyses, of the study were:
1.2.1 The first objective was to determine the effect of continuous therapeutic ultrasound applied at 0.2 W.cm\(^{-2}\) on radial artery blood flow (m.s\(^{-1}\)) and radial artery lumen diameter (mm) at baseline, at four minutes of application and one-minute after application.

1.2.2 The second objective was to determine the effect of pulse therapeutic ultrasound applied at 0.2 W.cm\(^{-2}\) on radial artery blood flow (m.s\(^{-1}\)) and radial artery lumen diameter (mm) at baseline, at four minutes of application and one-minute after application.

1.2.3 The third objective was to determine the effect of continuous therapeutic ultrasound applied at 1.5 W.cm\(^{-2}\) on radial artery blood flow (m.s\(^{-1}\)) and radial artery lumen diameter (mm) at baseline, at four minutes of application and one-minute after application.

1.2.4 The fourth objective was to determine the effect of pulse therapeutic ultrasound applied at 1.5 W.cm\(^{-2}\) on radial artery blood flow (m.s\(^{-1}\)) and radial artery lumen diameter (mm) at baseline, at four minutes of application and one-minute after application.

1.2.5 The fifth objective was to determine the effect of sham therapeutic ultrasound applied at 0 W.cm\(^{-2}\) on radial artery blood flow (m.s\(^{-1}\)) and radial artery lumen diameter (mm) at baseline, at four minutes of application and one-minute after application.

1.2.6 To determine the correlation between the radial artery blood flow (m.s\(^{-1}\)) and radial artery lumen diameter (mm) for each of the three time periods for each of the five groups.

1.3 HYPOTHESES OF THE STUDY

Based on the conflicting results of Clemente et al. (1992) and Fabrizio et al. (1996) on the effect of therapeutic and sham ultrasound on blood flow in a muscular artery, the Null Hypothesis (H\(_0\)) was set which stated there would be no significant association between pulse, continuous or sham ultrasound and radial artery blood flow.
With respect to an association between continuous, pulse or sham ultrasound and radial artery lumen diameter, the Null Hypothesis ($H_0$) was set which stated there would be no significant association between these interventions and radial artery lumen diameter.

With respect to a correlation between the radial artery blood flow and radial artery lumen diameter, the Null Hypothesis ($H_0$) was set which stated there would be no significant association between these two parameters.

### 1.4 SCOPE OF THE STUDY

The results of 50 healthy, asymptomatic volunteers, between the ages of 18-38 years, are reported in this dissertation. All subjects provided written informed consent prior to participating in this study. The subjects were randomly allocated into one of five intervention groups (A-E). Group A received continuous ultrasound at 0.2 W.cm$^{-2}$ for five minutes, Group B received pulse ultrasound at 0.2 W.cm$^{-2}$ for five minutes, Group C received continuous ultrasound at 1.5 W.cm$^{-2}$ for five minutes, Group D received pulse ultrasound at 1.5 W.cm$^{-2}$ for five minutes and Group E received sham ultrasound at 0 W.cm$^{-2}$ for five minutes. Baseline radial artery blood flow and radial artery lumen diameter readings were taken prior to the commencement of the therapeutic or sham ultrasound application using a Doppler ultrasound. At four minutes of application (i.e. during the therapeutic or sham ultrasound application), another set of blood flow and arterial lumen diameter measurements were taken. The final blood flow and arterial lumen diameter measurements were taken one minute after the therapeutic or sham ultrasound application was stopped.
CHAPTER TWO

LITERATURE REVIEW

2.1 INTRODUCTION
Therapeutic ultrasound is a widely-used modality in the treatment of various musculoskeletal conditions (Dyson, 1989; Ter Haar, 1999; Robertson and Baker, 2001) as it is useful in the treatment of soft tissue healing and repair, scar tissue injuries and joint contractures, chronic inflammation, bone healing and pain reduction (Ecternach, 1965; McDiarmid and Burns, 1987; Dyson, 1989; Ziskin et al., 1990). One of the mechanisms put forth to explain the healing effect of therapeutic ultrasound is increased blood flow to the area of the lesion (Hasson et al., 1990).

2.2 DESCRIPTION AND STRUCTURE OF ARTERIES
The arteries of the human body transport blood away from the heart and distribute it to the rest of the body. These blood vessels are divided into three types according to Moore and Dalley (2005) viz. elastic arteries, muscular arteries and arterioles and consist of three concentric layers or tunicae viz. the tunica intima, tunica media and tunica adventitia (Standring, 2005). Elastic arteries are the largest type and enable the body to maintain blood pressure in the arterial system between contractions of the heart largely due to their elasticity (Moore and Dalley, 2005). The intima in elastic arteries is composed of an endothelium resting on a basal lamina. The endothelial cells are flat, elongated and polygonal in outline, with their long axes parallel to the direction of blood flow. The media of elastic arteries is separated from the intima by a prominent internal elastic lamina. The structure of the media is markedly layered in which fenestrated layers of elastin alternate with interlamellar muscle cells, collagen and fine elastic fibres. The adventitia of elastic arteries contains flattened fibroblasts with long, thin processes, macrophages and mast cells, nerve bundles and lymphatic vessels in addition to collagen and elastic fibres (Standring, 2005).

Muscular arteries have a predominance of smooth muscle in the media. A distinct, thin-layered internal elastic lamina is present. The media is separated from the adventitia by an external elastic lamina, while the adventitia of muscular arteries is composed mainly of collagenous connective tissue (Standring, 2005). Arterioles are the smallest type and have fairly narrow lumina. The tunica intima of arterioles is very thin and consists of the
endothelial lining, a thin, but distinct internal elastic lamina and little collagenous connective tissue. The tunica media has smooth muscle cells in six or less concentric layers and the tunica adventitia merges with the surrounding connective tissues and can be as thick as the tunica media (Wheater et al., 1987).

2.3 ANATOMY OF THE RADIAL ARTERY

2.3.1 Embryology of the Radial Artery
The vascular pattern of a limb changes mainly through angiogenesis as the limb develops (Moore and Persaud, 2008). The primary artery to the arm is axially positioned and becomes the main subclavian-axillary-brachial trunk proximally (Patten, 1968). It then persists below the elbow as the common interosseous artery (Moore and Persaud, 2008). The brachial artery and its branches to the shoulder and elbow regions develop at a later stage as new offshoots of the primary axial vessel (Patten, 1968). The radial and ulnar arteries develop later as a branch of the brachial artery (Moore and Persaud, 2008).

2.3.2 Origin of the Radial Artery
The arch of the aorta commences posterior to the second right sternocostal joint at the level of the sternal angle (Standring, 2005). The brachiocephalic trunk is the largest and first branch of the aortic arch. It ascends superolaterally to reach the right side of the trachea and right sternoclavicular joint and divides into the right subclavian and the right common carotid arteries. The left subclavian artery arises as the third branch of the arch of the aorta. The subclavian artery continues as the axillary artery which begins at the lateral border of the first rib and ends at the inferior border of the teres major muscle (Moore and Dalley, 2005). Thereafter, it continues as the brachial artery as it crosses the distal edge of the posterior axillary fold (Standring, 2005). It then divides into the radial and ulnar arteries under the bicipital aponeurosis (Moore and Dalley, 2005).

2.3.3 Course and Relations of the Radial Artery
Medial to the neck of the radius, the radial artery passes under the fleshy belly of the brachioradialis muscle and then the rest of the artery is superficial and covered by the superficial and deep fascia. It lies upon the tendon of the biceps brachii, the supinator, the pronator teres, the radial origin of the flexor digitorum sublimis, the flexor pollicis longus, the pronator quadratus and the lower end of the radius (Standring, 2005). In the middle third of its course, the radial nerve lies in proximity to the lateral side of the artery. The radial artery is accompanied by a pair of venae comitantes throughout its course (Standring, 2005). It passes on to the dorsal aspect of the wrist by passing between the radial collateral ligament of the wrist and tendons of the abductor pollicis longus and
extensor pollicus brevis. It then passes from the upper end of the first interosseous space between the heads of the dorsal interossei and transversely across the palm between the adductor pollicis obliquus and adductor pollicis transverses. It anastomoses with the deep volar branch of the ulnar artery at the base of the fifth metacarpal bone (Standring, 2005). The radial artery, therefore, courses within three regions of the upper extremity viz. the forearm, wrist and hand (Moore and Dalley, 2005).

2.3.4 Anomalous Variations of the Radial Artery
There may be variations in the origin of the radial artery; it could have a high origin due to persistent duplication or precocious bifurcation of the brachial artery and the presence of a superficial dorsal ramus in the forearm (Drizenko et al., 2001). The brachial artery may divide at a more proximal level than usual resulting in the radial and ulnar arteries commencing near the middle of the arm (Moore and Dalley, 2005). Yoo et al. (2005) reported a high origin of the radial artery in 28 cases (i.e. 2.4%) in a study involving the anatomic consideration of the radial artery. They also reported the presence of a double radial artery in two cases and a double brachial artery in six cases.

2.4 RADIAL ARTERY DIAMETER
The diameter of the radial artery was in the approximate range of 2-3 mm as reported by Shima et al. (1996), Yoon (1998), Yoo et al. (2005), Ku et al. (2006) and Loh et al. (2007) (Table 2.1). Yoon (1998) reported that the diameter was larger in males than in females. This was corroborated later by Yoo et al. (2005) who reported that the mean (± SD) radial artery diameter to be 2.69 (± 0.40) mm in men and 2.43 (± 0.38) mm in women. Shima et al. (1996) reported that the mean (± SD) length of the radial artery was 18.1 (± 1.7) cm.

Table 2.1 Studies that have reported on the diameter of the radial artery

<table>
<thead>
<tr>
<th>Reference</th>
<th>Mean ± SD (mm)</th>
<th>Method</th>
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</thead>
<tbody>
<tr>
<td>Shima et al. (1996)</td>
<td>2.3 ± 0.5</td>
<td>Stereoscopic microscope and a digital measuring system</td>
</tr>
<tr>
<td>Yoon (1998)</td>
<td>2.7 ± 0.4</td>
<td>2-D ultrasonography</td>
</tr>
<tr>
<td>Yoo et al. (2005)</td>
<td>2.6 ± 0.4</td>
<td>2-D ultrasonography</td>
</tr>
<tr>
<td>Ku et al. (2006)</td>
<td>2.3 ± 0.3</td>
<td>High resolution ultrasonography</td>
</tr>
<tr>
<td>Loh et al. (2007)</td>
<td>2.4 ± 0.5</td>
<td>Duplex Doppler ultrasonography</td>
</tr>
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</table>

*2-D = Two-dimensional*

2.5 FACTORS AFFECTING RADIAL ARTERY DIAMETER
In 2007, Loh et al. reviewed the duplex Doppler ultrasonography scans of the left radial artery of 327 patients over a two-year period. They reported that gender (i.e. males),
hypertension and high lipid levels in the blood positively affected radial artery size, but increasing age and diabetes mellitus negatively affected the size. Khder et al. (1997) had earlier reported that hypertensive patients had larger lumenal diameters than non-hypertensive individuals. Loh et al. (2007) also reported that the size of the radial artery was not significantly influenced by race, smoking and renal failure.

2.6 BLOOD AND ITS CONSTITUENTS
“Blood is an opaque fluid with a viscosity greater than that of water and a specific gravity of c.1.06 at 15°C” (Standring, 2005). It is composed of 55% plasma and 45% cells (Marieb, 2006). The constituents of plasma include water, salts, plasma proteins, nutrients, hormones, waste products of metabolism and respiratory gases. The different cell types include erythrocytes, leukocytes, and platelets (Pocock and Richards, 2006). Erythrocytes are biconcave-shaped disc-like cells and are responsible for the transportation of oxygen to all cells in the body. The leukocytes are classified in two major groups viz. granulocytes and agranulocytes which are important for defense against disease. Platelets are required for normal blood clotting as they initiate the clotting cascade (Marieb, 2006).

2.7 CHARACTERISTICS OF BLOOD
The color of blood varies as it depends on its oxygen content. Blood colour varies from scarlet indicating that it is rich in oxygen to dull red indicating poor oxygen content (Marieb, 2006). It is slightly alkaline with a pH between 7.35 and 7.45 and a temperature of about 38°C which is usually higher than that of body temperature (Tortora and Derrickson, 2006). The volume of blood is usually five liters in a normal adult and accounts for approximately eight percent of the body weight (Pocock and Richards, 2006).

2.8 BLOOD PRESSURE
Guyton and Hall (2006) defined blood pressure as “the force exerted by the blood against any unit area of the vessel wall” which was measured in millimeters of mercury (mmHg). Pressure in the aorta, brachial and other large arteries rise to a peak value of about 120 mmHg in an adult during each cardiac cycle, known as the systolic pressure and drop to a minimum of about 80 mmHg, known as the diastolic pressure. The arterial or blood pressure is reflected as the systolic pressure over the diastolic pressure e.g. 120/80 mmHg (Guyton and Hall, 2006). The pulse pressure is the difference between the systolic and diastolic pressures (Ackermann, 2004) and is about 40 mmHg. The pulse pressure is affected by two factors viz. the stroke volume output of the heart and aortic stiffness (Ackermann, 2004).
There are two main factors that influence blood pressure i.e. central and peripheral factors (Davies et al., 2001). The central factors include cardiac output (CO) (Hirofumi, 2006) and heart rate (HR) and the peripheral factors include total peripheral vascular resistance (TPR), blood volume (Hirofumi, 2006) and elasticity of blood vessels (Davies et al., 2001). The action of the heart affects blood pressure through stroke volume (SV) and CO. Cardiac output refers to the quantity of blood pumped into the aorta each minute by the heart (Guyton and Hall, 2006) while SV refers to the amount of blood pumped out of each ventricle per beat (Ganong, 2001). The CO is the product of the SV and the HR (Pocock and Richards, 2006) as shown in the following equation:

\[ CO = SV \times HR \]

An increase in the CO results in an increase in the blood pressure (Pocock and Richards, 2006). Peripheral resistance, which is the friction between the blood and the walls of the blood vessel, is another factor that affects blood pressure.

There are three main sources of TPR viz. blood vessel diameter, blood viscosity and total vessel length (Sherwood, 2001). As the diameter of a blood vessel is reduced, a greater proportion of the fluid is in contact with the walls of the vessel leading to an increase in resistance to flow and a subsequent increase in pressure. Fluid viscosity is related to the thickness of a fluid and the greater the viscosity, the less easily molecules slide past each other and the more difficult it is to initiate movement of the fluid and to keep it moving. Due to this resistance to flow, more pressure is required to pump the same volume of viscous fluid (Sherwood, 2001).

The vessel length and radius determine the surface area of contact with blood. If the vessel length is large, the surface area increases and, hence, the resistance also increases leading to an increase in blood pressure (Sherwood, 2001). A healthy elastic artery expands and absorbs the shock of the systolic pressure. The elastic recoil of the vessel then maintains continued flow of blood during diastole. During disease e.g. atherosclerosis, the arteries become calcified and rigid and cannot expand during the pulse wave of systolic pressure through them resulting in higher pressures in the arterial walls. If there is a greater volume of fluid in a blood vessel, then more fluid is pressing against the walls, leading to greater pressure in the arterial wall (Kindlen et al., 2003). Another factor that affects blood pressure is the vessel length (Kindlen et al., 2003) which is directly proportional to resistance. Therefore, a vessel that has a length that is double that of another vessel in turn has twice the resistance to flow. Since vessel length is
known not to change significantly in vivo, it is, therefore, considered to be a constant (Klabunde, 2005).

The regulation of blood pressure is essential to maintain adequate blood supply to the heart and brain (Ackermann, 2004). Blood pressure is regulated by short-term (mainly neural) and long-term mechanisms (mainly hormonal) (Kindlen et al., 2003; Pocock and Richards, 2006). The baroreceptor mechanism which has sensors in the wall of the carotid sinus and aortic arch is the main short-term regulator of blood pressure (Ackerman, 2004; Guyton and Hall, 2006). Baroreceptors are mechanoreceptors which have inhibitory effects that decrease sympathetic activity and increase parasympathetic activity (Kindlen et al., 2003). They respond to an increase in stretching of the vessel wall (Kindlen et al., 2003). An increase in action potential frequency resulting from stretching of the arterial walls due to an increase in pressure results in decreased sympathetic and increased parasympathetic stimulation of blood vessels and a decrease in blood pressure (Kindlen et al., 2003). A decrease in blood pressure causes a decrease in the frequency of action potentials, increases sympathetic stimulation of blood vessels and increases sympathetic stimulation of the heart resulting in increased blood pressure (Kindlen et al., 2003). The kidneys play a role in the long-term regulation of blood pressure (Sharma, 1992; Ackermann, 2004) by controlling fluid volume by excreting salt and water in a controlled manner in order to effect a decrease in high arterial pressure (Guyton and Hall, 2006).

Hormonal mechanisms that regulate blood pressure include the catecholamines, adrenaline and noradrenaline, which are secreted by the adrenal medulla (Pocock and Richards, 2006) and act on adrenoreceptors alpha (α) and beta (β). When catecholamines interact with α-adrenoreceptors, there is resultant vasoconstriction which in turn increases the CO (Sharma, 1992) whilst any interaction with the β-adrenoreceptors results in vasodilatation (Pocock and Richards, 2006). Since noradrenaline has a greater affinity for the α-adrenoreceptors, it has more of a vasoconstriction effect than adrenaline (Pocock and Richards, 2006).

Angiotensin II, a powerful vasoconstrictor, is released when arterial blood pressure is low (Klabunde, 2005). Angiotensin I is formed when renin released into the blood acts upon angiotensinogen. Thereafter, angiotensin-converting enzyme (ACE) from the vascular endothelium forms angiotensin II by cleaving off two amino acids. ACE is mainly found in the capillaries of the lung, but also in other tissues such as the heart and brain (Klabunde, 2005; Guyton and Hall, 2006). Its central effects are effected by increasing sympathetic
nerve activity while its peripheral effects are effected by the release of noradrenaline (Davies et al., 2001). It also stimulates the release of aldosterone from the adrenal cortex which in turn favours sodium and water reabsorption by the kidneys helping to restore blood pressure (Davies et al., 2001). Vasopressin, which is formed in the hypothalamus and secreted from the posterior pituitary gland, causes widespread vasoconstriction when blood pressure drops (Davies et al., 2001; Pocock and Richards, 2006). Atrial natriuretic peptide (ANP), which is secreted by the atrial myocytes, plays a role in decreasing the sensitivity of vascular smooth muscle to the angiotensin-aldosterone system by acting to oppose the changes effected by aldosterone (Pocock and Richards, 2006). These hormones are, therefore, physiologically involved in the controlling blood volume and maintaining arterial blood pressure on a long-term basis (Davies et al., 2001; Pocock and Richards, 2006).

2.9 BLOOD FLOW AND ITS REGULATING FACTORS

The blood flow at any point in circulation refers to the volume of blood that passes that point during a unit of time and is normally measured in milliliters per minute (Guyton and Hall, 2006).

Blood flow in blood vessels is usually laminar (Ku, 1997) which refers to a thin layer of blood within the blood vessel which is in contact with the vessel wall and does not move. A low velocity is present in the next layer within the vessel and the next layer has a higher velocity and so forth. The greatest velocity is present in the center of the stream (Ganong, 2001). Another type of flow is turbulent flow which refers to blood flowing in all directions in the vessel (Guyton and Hall, 2006).

Poiseuille's Law describes the control of blood flow by taking into account the viscosity of blood together with the vessel length and radius as shown by the following equation:

\[ Q = \frac{(L \times V)}{r^4} \]

whereby \( Q \) is the laminar flow, \( L \) is the vessel length, \( V \) is the viscosity of the blood and \( r \) is the vessel's radius (Davidovits, 2007).

Two physical factors determine blood flow through a vessel viz. the pressure difference between the two ends of the vessel, which is the force that pushes the blood through the vessel, and the impediment to blood flow through the vessel which is known as vascular resistance (Guyton and Hall, 2006). The blood flow is determined by dividing the pressure
difference between the two ends of the vessel ($\Delta P$) over the resistance to flow ($R$). The pressure difference between the two ends of the vessel ($\Delta P$) is calculated by subtracting the pressure at the end of the vessel ($P_2$) from the pressure at the origin of the vessel ($P_1$):

$$\Delta P = P_1 - P_2$$

The following formula is used to determine blood flow viz.

$$F = \Delta P / R$$

Whereby, $F$ represents the blood flow (Guyton and Hall, 2006).

There are two mechanisms of blood flow control viz. the acute and long-term control. The acute control produces rapid changes in local vasodilation and vasoconstriction of the arteries, metarterioles and precapillary sphincters, whereas long-term control results from changes that occur over a number of days, weeks or months due to an increase or decrease in the physical size and numbers of actual blood vessels supplying the tissues (Guyton and Hall, 2006).

### 2.9.1 Mechanisms of Vasoconstriction and Vasodilation

A vasoconstrictor is any substance that acts to cause narrowing of the lumen of blood vessels in the body (vasoconstriction) while a vasodilator is a substance that causes the lumen of blood vessels in the body to become wider (vasodilation) (Ganong, 2001; Klabunde, 2005).

#### A. Vasoconstriction

Sympathetic neurons are found in the tunica media of arteries (Tortora and Derrickson, 2006). If there is sympathetic stimulation, the smooth muscle contracts resulting in vasoconstriction (Tortora and Derrickson, 2006). Vasoconstrictor substances include adrenaline, noradrenaline, angiotensin, vasopressin, serotonin, prostaglandins and endothelin (Solomon et al., 1990; Guyton and Hall, 2006). Adrenaline and noradrenaline are secreted in the blood when the sympathetic nervous system is stimulated by stress (Guyton and Hall, 2006; Pocock and Richards, 2006). Angiotensin II causes strong vasoconstriction especially in the small arterioles to increase the TPR and arterial pressure (Guyton and Hall, 2006). An even more powerful vasoconstrictor called vasopressin is produced by the hypothalamus and released from the posterior pituitary
Prostaglandin synthesis occurs as a result of tissue injury which causes the cell membranes to release arachidonic acid. Some of these prostaglandins are responsible for vasoconstriction (Solomon et al., 1990). Endothelin which is present in the vascular endothelial cells is released in response to tissue damage, blood vessel injury or the injection of a destructive chemical into the blood (Guyton and Hall, 2006). Following any damage to the blood vessels, endothelin is released locally and vasoconstriction results to prevent excessive bleeding from the arteries during crushing injuries (Ganong, 2001; Guyton and Hall, 2006). Following injury and during the clotting process, platelet aggregation releases serotonin which controls bleeding and causes vasoconstriction (Solomon et al., 1990). When the body temperature is too low, the sympathetic centers in the posterior hypothalamus are stimulated to cause vasoconstriction of the skin blood vessels in order to increase the body temperature (Guyton and Hall, 2006).

**B. Vasodilation**

When there is a decrease in sympathetic stimulation or when chemicals such as hydrogen ions (H\(^+\)), lactic acid and nitric oxide are present in blood, the smooth muscle fibers relax causing widening of the lumen (Tortora and Derrickson, 2006). The most important vasodilators are kinins (mainly bradykinin), histamine and certain prostaglandins (Solomon et al., 1990; Guyton and Hall, 2006). The blood and tissue fluids contain globulin kininogen which liberate the kinins (Solomon et al., 1990; Guyton and Hall, 2006) which are responsible for increased capillary permeability, arteriolar smooth muscle relaxation and venule constriction (Solomon et al., 1990). Histamine-release from mast cells and basophils occurs in the presence of tissue damage, inflammation or an allergic reaction (Guyton and Hall, 2006). It increases capillary permeability allowing for fluid and plasma protein leakage into the tissues and has a vasodilator effect on the arterioles (Guyton and Hall, 2006). When the body temperature is too high, the skin blood vessels vasodilate due to the inhibition of the sympathetic centers in the posterior hypothalamus (Guyton and Hall, 2006). Localised heat induces vasodilation in arteries (Lemaire et al., 1977; Davison et al., 2004) resulting in increased localised blood flow called hyperaemia (Sherwood, 2001). Baker and Bell (1991) demonstrated that blood flow increased to the calf region during application of a heat-pack to that area.

**2.10 ASSESSMENT OF BLOOD FLOW**

There are invasive and non-invasive methods to measure peripheral blood flow within a blood vessel.
2.10.1 Invasive Methods

A) Venous Drainage

Although this method was mentioned by Brugmans et al. (1977) under invasive methods for measuring peripheral blood flow no further information regarding its role in the evaluation of peripheral blood flow was available.

B) Indicator Dilution

Any substance that mixes readily with blood, whose concentration can be determined in the blood after mixing and does not produce side-effects can be used as an indicator (Panday and Kumar, 2007). This includes dyes, radioisotopes and electrolytes (Meier and Zierler, 1954). Isotonic saline is the indicator that’s most frequently used today (Panday and Kumar, 2007). It is injected into the blood at a temperature less than that of the body temperature (Cromwell et al., 1980). The indicator is injected at the upstream then moved to downstream where the concentration of indicator is observed after mixing in the mixing chamber (Meier and Zierler, 1954).

C) Electromagnetic Flow Measurement

Magnetic blood flow meters are used to measure blood flow by being applied external to the vessel. These are based on the principle of magnetic induction which occurs when an electrical conductor is passed through a magnetic field resulting in a voltage being induced in the conductor proportional to its velocity of movement (Cromwell et al., 1980). These are typically used during surgery as they are placed in exposed blood vessels (Panday and Kumar, 2007).

2.10.2 Non-Invasive Methods

A) Plethysmography

Plethysmography has been used to record volume change in a tissue (Hyman and Winsor, 1961). The forearm is sealed in a watertight chamber and a volume recorder is used to measure the displacement in the water due to changes in the volume of the blood which reflects changes in the amount of blood and its interstitial fluid (Cromwell et al., 1980; Webster, 1998). In 1905, Brodie and Russell described the first flow measurements using venous occlusion plethysmography which disregarded the distribution, origin and change of flow in order to register total flow during each time unit (Brugmans et al., 1977).

Hiatt et al. (1989) conducted studies on five normal subjects to investigate whether the cuff pressure required for venous occlusion plethysmography decreased arterial inflow.
When Doppler velocity measurements and plethysmography were compared, the arterial inflow using the plethysmography was less than that of the Doppler measurements. Earlier studies (Landowne and Katz, 1942; Wilkins and Bradley, 1946) reported that inflation of a cuff on an extremity to low pressures for venous occlusion caused a reduction in arterial diameter and flow velocity. Landowne and Katz (1942) stated that causes of error were due to local tissue deformation at cuff inflation and to the volume recording technique. The validity of the results was, therefore, dependent on appropriate cuff pressure (Landowne and Katz, 1942; Wilkins and Bradley, 1946). Robinson and Buono (1995) stated that although plethysmography could reliably measure total limb volume changes, it did “not reflect isolated flow changes in specific tissues”.

B) Calorimetric

This is a thermal method where a thermometer measures heat elimination from a given volume of finger and thereafter converts it to blood flow (Woodcock, 1976). The phalanx is placed in a calorimeter with water at a constant temperature of 29°C while an electrically heated cloth wrapped around the arm prevents pre-cooling of arterial blood reaching the digits (Coffman, 1989). Stewart (1911) described a calorimetric method based on the assumption that the heat lost by the hand is the same as that which is gained by the calorimeter and its contents. Its value to determine blood flow through the extremities has been doubted (Sheard, 1926; Harris and Marvin, 1927). Sheard (1926) disputed Stewart’s (1911) theory by stating that the rate of heat removal from the immersed limb depended on the blood flow, the number of skin blood vessels at a certain time, the number of functional capillaries and their degree of vasodilation or vasoconstriction. Harris and Marvin (1927) inserted a thermocouple into a vein in the hand which was immersed in water. They found that the temperature varied between the venous blood and that of the fluid in which the hand had been placed. Although it is non-invasive as well as transcutaneous, calorimetry, however, is a limited instrument as the blood flow can be altered by the water temperature in the calorimeter (Woodcock, 1976).

C) Ultrasonic Flowmeters

An ultrasonic flowmeter is used to measure blood flow rate by being applied external to the vessel (Webster, 1998). A minute piezoelectric crystal mounted at one end in the wall of the device (Webster, 1998), when energized with an appropriate electronic apparatus, transmits ultrasound at a frequency of several hundred thousand cycles per second [megahertz (MHz)] downstream along the flowing blood. Red blood cells in the flowing blood reflect a portion of the sound which then travels backwards from the blood cells towards the crystal. Since the red blood cells are moving away from the crystal, the
reflected waves have a lower frequency than the transmitted wave (Cromwell et al., 1980). There are two types of ultrasonic flowmeters viz. transit-time type and Doppler-shift type (Woodcock, 1976).

D) Laser-Doppler Flowmetry
Instead of sound, a monochromatic light is delivered through an optical fiber from a laser (Coffman, 1989). This technique uses high frequencies of visible and infrared light of short wavelengths to measure tissue perfusion by using the Doppler shifts imparted by red blood cells to light (Shepherd and Öberg, 1990).

E) Doppler Ultrasound
A Doppler ultrasound is a reliable and effective (Kalsner, 1983) non-invasive technique for detecting and measuring the velocity of moving structures within the body including blood (Evans and McDicken, 2000). The Doppler effect refers to a change in the frequency of sound waves reflected by a moving object (Bentley, 2004). A Doppler ultrasound estimates how fast blood flowed by measuring the rate of change in its pitch (frequency). This test is used as an alternative to more invasive procedures such as arteriography and venography for the evaluation of an injury to the arteries or for the monitoring of arterial reconstruction and bypass grafts (Sheps, 2007).

Doppler ultrasound is utilised in different modes viz. pulse ultrasound, continuous Doppler, pulse Doppler or Range-gated pulse Doppler. The type commonly used for blood flow measurements is the continuous Doppler ultrasound (Cromwell et al., 1980). Two-dimensional ultrasound images are made up of a series of thin image slices, with only one slice being visible at any one time to create a flat-looking picture (Evans and McDicken, 2000). Three-dimensional ultrasound refers to thousands of image slices in a series known as volume of echoes which are stored digitally and produce life-like images (Evans and McDicken, 2000). The four types of Doppler ultrasound are bedside or continuous wave Doppler, duplex Doppler, color Doppler and power Doppler (Grainger et al., 2001).

Continuous wave Doppler uses the change in the pitch of the sound waves to provide information about blood flow through a blood vessel and for the evaluation of blood flow through an area that may be blocked or narrowed (Grainger et al., 2001). Duplex ultrasound determines how blood moves through arteries and veins and it combines conventional ultrasound with Doppler ultrasound (Grainger et al., 2001). Color Doppler utilises standard ultrasound methods to produce a graphic of a blood vessel which is then converted by a computer into colors that are overlaid on the image of the blood vessel
Power Doppler is a more recent technique which is up to five times more sensitive in detecting blood flow than color Doppler and is most commonly used to evaluate blood flow through vessels within solid organs (Evans and McDicken 2000). Blood flow in individual blood vessels is most commonly evaluated by combining color Doppler with duplex Doppler. Together, they are able to provide better information on the direction and speed of blood flow than when these techniques are used individually (Grainger et al., 2001).

Previous studies using Doppler ultrasound on human subjects had not reported any adverse reactions in terms of safety (Clemente et al., 1992; Fabrizio et al., 1996).

2.11 ULTRASOUND
The definition of ultrasound is a sound wave of a frequency of 20 000 Hz or greater (Hedrick, 1995) which is above the frequency for human hearing (Shoh, 1988). Ultrasound is used for both medical (Draper and Prentice, 2005) and industrial (Shoh, 1988) purposes.

2.12 THERAPEUTIC ULTRASOUND
Therapeutic ultrasound refers to ultrasound which is used as a therapeutic modality in a clinical setting rather than a diagnostic tool (Prentice, 1994). It is widely utilized by physiotherapists (Dyson, 1989; Ter Haar, 1999) and chiropractors (Nussbaum, 1997; Daniel and Rupert, 2003) as an adjunctive physical therapy modality. Therapeutic ultrasound is administered in two wave forms viz. pulse and continuous (Draper and Prentice, 2005). When continuous wave ultrasound is used, the intensity remains constant throughout the application and ultrasound energy is produced one hundred percent of the time, whereas, with pulse ultrasound the intensity is periodically interrupted and no ultrasound energy is produced during the off-period (Draper and Prentice, 2005). The general indication for the use of pulse ultrasound is to facilitate the healing of soft tissue injury in the inflammatory and proliferative phases (of tissue healing) while continuous ultrasound is used for pain control in chronic pain and/or inflammatory conditions (Kitchen and Bazin, 1996).

2.12.1 Clinical Uses
The primary purpose of therapeutic ultrasound is as a non-invasive modality in the treatment of tendonitis, bursitis, sprains and strains (Echternach, 1965; Makuloluwe and Mouzas, 1977; Gorkiewicz, 1984). It is also used in the treatment of intervertebral disc disease and arthritic conditions (Nwuga, 1983; Casimiro et al., 2002). Despite the use of
therapeutic ultrasound for the treatment of these conditions for many decades, its effectiveness remains to be verified (Robertson and Baker, 2001). In their review of 35 randomised clinical trials between 1975 and 1999, Robertson and Baker (2001) reported that there was little evidence that active therapeutic ultrasound was better than placebo in promoting soft tissue healing in the management of a wide range of musculoskeletal injuries. Amongst the reasons for this finding were a broad spectrum of patient conditions and the considerable variation in the dosages, often for no reason, in several studies. Other studies (Ecternach, 1965; Dyson et al., 1968; McDiarmid and Burns, 1987; Dyson, 1989; Dyson, 1990; Pilla et al., 1990; Ziskin et al., 1990) had, however, shown that therapeutic ultrasound was useful in soft tissue healing and repair, breakdown of scar tissue and joint contracture, chronic inflammations, bone healing and pain reduction. One of the mechanisms put forth to explain the healing effect of therapeutic ultrasound was increased blood flow to the area of the lesion (Hasson et al., 1990).

2.12.2 Safety of Therapeutic Ultrasound

Contraindications to therapeutic ultrasound have been reported in previous publications (Lehmann and De Lateur, 1990; Dyson, 1985). Ultrasound is not to be applied therapeutically to any patient with obtunded reflexes or to any area with diminished pain or heat sensitivity (Oakley, 1978; Lehmann and De Lateur, 1990). Pregnant patients are not to receive ultrasound therapy in any area of the body which was likely to result in exposure to the fetus due to possible overheating of the fetus which is at particularly high risk during the first trimester (Oakley, 1978; Lele, 1979). Any area of diminished blood circulation should not undergo irradiation, except at low intensities at which wound healing can occur (Oakley, 1978; Lehmann and De Lateur, 1990). Therapeutic ultrasound application to the spinal cord, brain, large subcutaneous peripheral nerves and reproductive organs is to be avoided (Oakley, 1978).

Neoplastic tissue is not to be irradiated as there is evidence that temperatures less than 42°C stimulated tumor growth or promoted metastases (Hynynen et al., 1981). The epiphyseal growth plates in children are to be avoided (Lehmann and De Lateur, 1990). Therapeutic ultrasound is not to be applied in the thoracic region if the patient has a cardiac pacemaker (Oakley, 1978). Patients with thrombophlebitis or other thromboembolic diseases are not to be treated with ultrasound since a partially disintegrated clot could result in an obstruction of the arterial supply to the brain, heart or lungs (Oakley, 1978).
Previous studies investigating the effects of therapeutic ultrasound on asymptomatic individuals had not reported any side-effects or adverse reactions to its use (Clemente et al., 1992; Fabrizio et al., 1996; Ware et al., 2001; Noble et al., 2007).

2.12.3 Biophysical Effects of Therapeutic Ultrasound

Numerous studies have been conducted on the biophysical effects of therapeutic ultrasound in vitro (Harvey et al., 1975; Fahnestock et al., 1989; Ramirez et al., 1997), which could be separated into thermal and non-thermal effects (Dyson, 1987; Kitchen and Partridge, 1990; Ter Haar, 1999). Continuous wave ultrasound was associated with the thermal effects while pulse wave ultrasound was associated with the non-thermal effects (Baker et al., 2001). Despite the difference in the mechanisms of action of pulse and continuous ultrasound, Ter Haar (1988) and Baker et al. (2001) reported that it was not possible to separate the two effects of heating and cavitation. Hogan et al. (1982b) had earlier reported that circulation improved on an ischemic rat muscle following the application of pulse ultrasound which was independent of the heating effect.

Although heating was shown to occur in both pulse and continuous ultrasound (MacDonald and Shipster, 1981; Sandler and Feingold, 1981; Williams, 1987), according to Dyson (1987), Ter Haar (1987), Kitchen and Partridge (1990), Lehmann and De Lateur (1990), Baker et al. (2001) and Johns (2002) it occurred more with continuous than pulse ultrasound.

A) Thermal Effects

A rise in tissue temperature was associated with the thermal effects of continuous ultrasound (Lehmann et al., 1978; MacDonald and Shipster, 1981; Sandler and Feingold, 1981; Fyfe and Bullock, 1985; Williams, 1987; Draper et al., 1995; Ashton et al., 1998; Chan et al., 1998). This rise in temperature was responsible for increased blood flow (Bickford and Duff, 1953; Paul and Imig, 1955; Dyson, 1987; Hasson et al., 1990), decreased pain (Patrick, 1966; Oakley, 1978; Dyson, 1987), increased collagenous tissue (ligaments, tendons, joint capsules, nerve roots) extensibility (Webster et al., 1980; Enwemeka et al., 1990), decreased joint stiffness (Lehmann and De Lateur, 1990), induction of a mild inflammatory response which decreased chronic inflammation (Dyson, 1987) and decreased muscle spasm (Draper et al., 1995; Reed and Ashigaka, 1997).

A study by MacDonald and Shipster (1981) using pulse or continuous ultrasound on isonated rabbit thighs demonstrated an increase in temperature. Other studies did not support the notion that ultrasound heated tissues adequately to produce the described
physiological effects (Imig et al., 1954; Stoller et al., 1983; Black et al., 1984). Stoller et al. (1983) conducted a study to heat ligaments using therapeutic ultrasound and reported no increase in joint laxity after ligament heating. Black et al. (1984) reported no increase in muscle peak torque following application of therapeutic ultrasound to the anterior tibial compartment. Lehmann et al. (1966), Lehmann and De Lateur (1990) and Johns (2002) on the other hand, considered that the degree of temperature rise should be significant enough in order for it to be considered therapeutic. Temperature increases of 2-3°C were shown to decrease pain and muscle spasm, increases of 1°C resulted in increased metabolism, decreased joint stiffness and increased collagen extensibility resulted from temperature increases of 4°C (Lehmann and De Lateur, 1990; Castel, 1993). Dyson (1987) and Draper et al. (1995), on the other hand, stated that the higher temperatures required for effective heating were possibly damaging to tissues.

B) Non-Thermal Effects
The non-thermal effects of ultrasound were described in previous studies (Nyborg, 1982; Dyson, 1987; Kitchen and Partridge, 1990). Ter Haar (1987) and Dyson (1987) divided the non-thermal effects into cavitation and acoustic microstreaming. Cavitation referred to the formation of gas-filled bubbles that expanded and then compressed (Dyson, 1987; Ter Haar, 1987). Two types of cavitation existed viz. stable or unstable (transient). Stable cavitation referred to a steady expansion and contraction of the bubbles while in unstable cavitation the bubbles collapsed due to large excursions (Dyson, 1987; Ter Haar, 1987). Local destruction of tissue and free radical production was thought to result from increased pressure and high temperatures produced at the site of the collapsing bubble (Dyson, 1987).

Microstreaming referred to “a steady circulation of fluid induced by radiation forces” (Dyson, 1987). High viscous stresses resulting from microstreaming could induce structural and functional changes in cell membrane (Dyson, 1987; Ter Haar, 1987). However, in the absence of cell membrane damage, microstreaming was of little therapeutic value due to the influx of calcium, sodium and other ions and metabolites that were required to accelerate the healing process (Dyson, 1987). Chapman et al. (1979) reported that these ionic changes could potentially change the tone of the smooth muscle wall in blood vessels. The physiological effects of cavitation and microstreaming included decreased pain (Patrick, 1978), mast cell degranulation (Dyson, 1982; Fyfe and Chahl, 1982), increased protein synthesis due to stimulation of fibroblast activity (Harvey et al., 1975; Webster et al., 1978; Young and Dyson, 1990a; Ramirez et al., 1997), bone healing (Duarte, 1983; Pilla et al., 1990), tissue regeneration (Dyson, 1987), altered cell
membrane function (Madsen and Gersten, 1961; Anderson and Barrett, 1981), increase in vascular permeability (Hogan et al., 1982b), increased tensile strength of collagen (Webster et al., 1980; Enwemeka et al., 1990) and increased angiogenesis (Hogan et al., 1982b; Young and Dyson, 1990b).

2.12.4 Blood Flow Effects of Therapeutic Ultrasound

An increase in blood flow following the application of ultrasound could produce desirable therapeutic effects (Draper et al., 1995). Increased blood flow is required for the delivery of oxygen, white blood cells and nutrients to the area of injury (Tortora and Grabowski, 2001) and the removal of metabolic waste products and tissue debris (Sherwood, 2001) in response to tissue damage. Increased blood flow following vasodilation could be due to histamine release from mast cells after injury (Maxwell, 1992; Sherwood, 2001). It was observed that if damaged tissues were exposed to ultrasound during the inflammatory phase of healing, there was an increase in blood flow (Dyson, 1987; Hasson et al., 1990). Degranulation of mast cells and subsequent histamine release following ultrasound application could result in haemodynamic changes (Fyfe and Chahl, 1982) which may explain why increased blood flow was observed following ultrasound application. However, it was uncertain whether this was due to the thermal or the non-thermal effects.

An increase in blood flow associated with a rise in temperature following therapeutic ultrasound intervention resulted in various desirable effects viz. reduced joint stiffness (Dyson, 1987; Ter Haar, 1999; Baker et al., 2001), increased cellular activity (Baker et al., 2001) and increased extensibility of collagenous structures (Draper et al., 1993; Warden and McMeeken, 2002).

An increase in blood flow from ultrasound application could reduce pain by removing pain metabolites irritating the receptor endings of afferent neurons (Maxwell, 1992; Nussbaum, 1997; Sherwood, 2001). Local blood flow increase relaxed spastic muscles and caused hypoalgesia (Hasson et al., 1990; Fabrizio et al., 1996; Cambier et al., 2001). Despite these reports, the results of the studies which have investigated the effect of therapeutic ultrasound on blood flow in animals and humans have been ambivalent as shown in Table 2.2.
Table 2.2  A summary of the studies which have investigated the effects of ultrasound on blood flow in animals and humans

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample</th>
<th>Area of application</th>
<th>Type of ultrasound</th>
<th>Tool</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bickford and Duff (1953)</td>
<td>Human subjects</td>
<td>F/A mm</td>
<td>3.0-3.5 W.cm²</td>
<td>VOP</td>
<td>↑ in BF</td>
</tr>
<tr>
<td>Paul and Imig (1955)</td>
<td>Dogs and human subjects</td>
<td>Dogs: femoral artery; humans: forearm</td>
<td>Dogs: 0.5 W.cm² for 15 min and 1 W.cm² for 15 min; Humans: 2 W.cm² for 20 min for ½ the subjects and the other ½ 3.0-3.5 W.cm²</td>
<td>Dogs: flowmetry; humans: VOP</td>
<td>Dogs: no change in BF for 0.5 W.cm² but significant ↑ in BF during last 5 min with 1 W.cm² (p &lt; 0.05) Humans: group that received 2 W.cm² and 3.0-3.5 W.cm² showed an ↑ in BF</td>
</tr>
<tr>
<td>Abramson et al. (1960)</td>
<td>16 male subjects</td>
<td>F/A</td>
<td>1 MHz between 0 – 30 W.cm² (2 stationery sound heads were used)</td>
<td>VOP</td>
<td>↑ in BF</td>
</tr>
<tr>
<td>Hogan et al. (1982a)</td>
<td>Rats</td>
<td>Cremaster mm</td>
<td>1.0 MHz (pulse) at 1.25, 2.5, 5.0 and 10.0 W.cm² for 5 min</td>
<td>Flowmetry</td>
<td>No significant change in BF and lumen diameter &lt; 10.0 W.cm² in the largest and 2nd order arterioles. Significant ↓ in BF and lumen diameter in smallest arterioles at 5.0 and 10.0 W.cm² (p &lt; 0.05)</td>
</tr>
<tr>
<td>Hogan et al. (1982b)</td>
<td>Rats</td>
<td>Ischaemic cremaster mm</td>
<td>1.0 MHz (pulse) at 2.5 W.cm² over a 1-3 week period</td>
<td>Flowmetry</td>
<td>↑ arteriolar BF in acute ischaemic mm.</td>
</tr>
<tr>
<td>Rubin et al. (1990)</td>
<td>Rats</td>
<td>Cremaster mm – normal and normoxic</td>
<td>Pulse at 2.5 and 5.0 W.cm²</td>
<td>Flowmetry</td>
<td>2.5 W.cm² = no significant changes in BF in normal tissue. BF was ↓ only in the normoxic tissue at 5 W.cm²</td>
</tr>
<tr>
<td>Baker and Bell (1991)</td>
<td>9 male subjects</td>
<td>Calf</td>
<td>5 W.cm² for 5 min</td>
<td>Impedance plethysmography</td>
<td>BF ↑ following U/S application</td>
</tr>
<tr>
<td>Clemente et al. (1992)</td>
<td>8 males and 6 females</td>
<td>Both heads of the left gastrocnemius mm</td>
<td>Continuous at 1.5 W.cm² for 5 min; pulse at 1.5 W.cm² for 5 min; sham at 0 W. cm²</td>
<td>A dual frequency, bi-directional Doppler ultrasound (left popliteal aa)</td>
<td>No significant change in BF</td>
</tr>
<tr>
<td>Robinson and Buono (1995)</td>
<td>10 healthy males and 10 females</td>
<td>Anterior F/A. Contra-lateral F/A was used for the control group</td>
<td>Continuous at 1.5 W.cm² for 5 min. Control at 0 W.cm²</td>
<td>F/A BF was measured using VOP and skin BF using laser Doppler flowmetry</td>
<td>No change in F/A BF but ↑ in skin BF</td>
</tr>
<tr>
<td>Fabrizio et al. (1996)</td>
<td>10 healthy males and 10 healthy females</td>
<td>The triceps surae mm</td>
<td>Group 1: 1MHz at 1.5 W.cm²; Group 2: 1MHz at 1.0 W.cm²; Group 3: 3 MHz at 1.2 W.cm²; Group 4: 3 MHz at 1 W.cm²; Group 5: sham U/S; Group 6: control</td>
<td>Dual frequency, bidirectional Doppler ultrasound (popliteal aa)</td>
<td>Groups 1 and 2 showed significant ↑ in BF velocity (p &lt; 0.05). Group 6 showed significant ↓ in BF velocity compared to Group 5 (p &lt; 0.05). No significant change in BF in Groups 3 and 4 (p &gt; 0.05)</td>
</tr>
</tbody>
</table>
Studies on animal models have produced varying results. Paul and Imig (1955) (Table 2.2) reported different changes in blood flow using two different ultrasound settings. Blood flow was not affected following ultrasound application at a low intensity of 0.5 W.cm\(^{-2}\). Hogan et al. (1982b) (Table 2.2) reported that pulse ultrasound increased blood flow independently of heating. Bickford and Duff (1953) reported that ultrasound produces heat which results in vasodilation of the local arterioles. Hogan et al. (1982a) (Table 2.2), on the other hand reported vasoconstriction of the small arterioles following ultrasound applications at 5.0 W.cm\(^{-2}\). They also demonstrated that repeated exposures of ultrasound over a one- to three-week period increased blood flow at a microscopic level rather than altering blood flow in larger vessels. They could not provide any explanation for the resultant arteriolar vasoconstriction that occurred. However, when Rubin et al. (1990) (Table 2.2) used the same intensity and duration of therapeutic ultrasound as Hogan et al. (1982b), they reported no change in blood flow with pulse ultrasound.

Human studies on ultrasound at tolerable intensities showed a decrease in skin temperature with ultrasound application (Bickford and Duff, 1953; Paul and Imig, 1955; Table 2.2) while other studies showed an increase in skin temperature following ultrasound application (Abramson et al., 1960; Ware et al., 2001). Using venous occlusion plethysmography to measure blood flow and iron-constantan thermocouples to measure temperature changes, Bickford and Duff’s (1953) (Table 2.2) results supported the theory that ultrasonic energy in tissues generated heat, which in turn caused local arteriolar relaxation. Treatments at high intensities showed a sustained increase in flow. They also observed that the rise in temperature in the skeletal muscles was of short duration due to rapid heat loss following hyperemia. Abramson et al. (1960) used thermocouples to record skin and muscle temperature changes on 14 subjects and observed a maximal increase of 0.9°C in both skin and muscle temperature after 16 and 17 minutes of treatment initiation respectively. Baker and Bell (1991) reported that blood flow in muscles could increase following ultrasound application only or in combination with cold therapy. The results of Bickford and Duff (1953), Paul and Imig (1955) and Abramson et al. (1960),

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Location</th>
<th>Ultrasound Parameters</th>
<th>Method</th>
<th>Additional Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ware et al. (2001)</td>
<td>8 healthy males and 6 healthy females</td>
<td>Mid-posterior calf</td>
<td>Continuous at 1.5 W.cm(^{-2}) for 10 min</td>
<td>Laser-Doppler flowmetry</td>
<td>↓ skin BF; No change in skin BF in contralateral calf</td>
</tr>
<tr>
<td>Noble et al. (2007)</td>
<td>5 healthy males and 5 healthy females</td>
<td>Lateral aspect of F/A</td>
<td>Control: no U/S; sham at 0.0 W.cm(^{-2}); 3 MHz pulse and continuous at 1.0 W.cm(^{-2}) for 6 min</td>
<td>Laser-Doppler flowmetry</td>
<td>Cutaneous BF ↑ with U/S</td>
</tr>
</tbody>
</table>

U/S = ultrasound; BF = blood flow; F/A = forearm; mm = muscle or musculature; aa = artery; ↓ = decrease/d; ↑ = increase/id; VOP = venous occlusion plethysmography; min = minutes
should, however, be viewed with caution as venous occlusion plethysmography measured total fluid volume changes in a limb (Fabrizio et al., 1996) and not specific flow changes in a specific tissue (Robinson and Bouno, 1995). The differences in the duration of the ultrasound application would also count for the inconsistent results of the various studies as Abramson et al. (1960) reported increased blood flow to the forearm after 18 to 21 minutes of therapeutic ultrasound application.

Robinson and Buono (1995) (Table 2.2) showed an increase in skin blood flow 15 minutes post-treatment and forearm blood flow five minutes post-treatment. There was no significant difference between the control and ultrasound-treated arms. The authors stated that one of the limitations of their study was their inability to monitor blood flow during ultrasound application. The intervention protocol of Ware et al. (2001) (Table 2.2) was thought to bring about a response in the superficial tissues. Skin temperature was measured using a thermistor and, although, skin surface temperature increased by \( \pm 1.4^\circ C \) after ten minutes of intervention, the dermal blood flow decreased by \( \pm 12 \% \). This was attributed to the thermal and non-thermal effects of ultrasound. Ware et al. (2001) concluded that an adequate vascular effect could not be demonstrated and the efficacy of therapeutic ultrasound to increase skin blood flow could be doubted. Noble et al. (2007) (Table 2.2) showed an increase in cutaneous blood flow with no significant difference in skin temperature with the use of pulse, continuous or sham ultrasound intervention. This physiological effect was possibly due to the massaging effect of the ultrasound probe together with the active ultrasound. Interestingly, although Noble et al. (2007) observed an increase in cutaneous blood flow following pulse ultrasound application, they did not attribute this to the thermogenic effect, but rather attributed it to a physiologic or non-thermal effect.

Clemente et al. (1992) and Fabrizio et al. (1996) (Table 2.2) conducted studies on muscular arteries using therapeutic ultrasound at varying intensities and modes. In the study of Clemente et al. (1992), blood flow was recorded three times at five-minute intervals before the commencement of the ultrasound application and also at three minutes into application, immediately after ultrasound and at one, three, five, ten and fifteen minutes post-application. Neither the pulse nor continuous mode ultrasound at 1.5 W.cm\(^{-2}\) altered blood flow in the artery. Fabrizio et al. (1996) showed a significant increase in arterial blood flow after sham intervention and with a frequency of one MHz at intensities of 1.0 and 1.5 W.cm\(^{-2}\) (Table 2.2). Furthermore, there was a significant decrease \((p < 0.05)\) in blood flow velocity in the sham group compared to other groups (Table 2.2). The sham ultrasound application had no significant effect on blood flow.
(Clemente et al., 1992), but when compared to controls, there was a significant difference (increase) (Fabrizio et al., 1996; Noble et al., 2007). This was attributed to the massaging effect of the ultrasound head (Fabrizio et al., 1996; Noble et al., 2007).

Some researchers (Maxwell, 1992; Nussbaum, 1997; Ter Haar, 1999) suggested that the increase in blood flow was due to vasodilation, which occurred by the release of chemical mediators or by an increase in temperature (i.e. thermal effect). However, the exact mechanism for an increase in peripheral blood flow remains unclear (Noble et al., 2007).

2.13 THE HAWTHORNE AND PLACEBO EFFECTS

2.13.1 The Hawthorne Effect

When human beings become aware that they are being observed, their behaviour may become altered resulting in a phenomenon called the Hawthorne effect (Mouton and Marais, 1994) which was first observed in Chicago's Western Electrical Company's Hawthorne Works in the 1920s and 1930s (Roethlisberger and Dickson, 1939; Mayo, 1993). Patients, especially those who participate in clinical trials, are not exempt from this phenomenon (McCarney et al., 2007) which was originally defined by Franke and Kaul (1978) as “an increase in worker productivity produced by the psychological stimulus of being singled out and made to feel important”. With respect to patients who participate in clinical trials, the Hawthorne effect refers to their response to treatment rather than any productivity (McCarney et al., 2007). Although, the Hawthorne effect is usually not factored in the design of many clinical trials, it is nonetheless “a component of the non-specific effects of trial participation” (McCarney et al., 2007). Some of the reasons put forth to explain the lack of quantification of the Hawthorne effect in most clinical studies include increased levels of clinical surveillance and extra attention by researchers which apply equally to both the treatment and control groups (McCarney et al., 2007). Increased participant compliance as a result of their being observed by the researchers was reported by Fiel et al. (2002) and Eckmanns et al. (2006). De Amici et al. (2000) and McCarney et al. (2007) observed that instructions given to participants in clinical trials contributed to the clinical significance of the Hawthorne effect.

2.13.2 The Placebo Effect

The placebo effect is used to determine the patient’s response to a sham therapy compared to an active one and is described by McConnell and Philipchalk (1992) as a “harmless, unmedicated treatment used for its psychological effect, often as a comparison with other treatments”. In most instances the placebo effect is utilised in pharmacological trials where the primary objective is to determine the efficacy of an active drug compared
to a closely-resembling sham or placebo drug. The participants are not aware of whether they are receiving an active or placebo drug which allows the researcher to measure the “physical effects independently of the participants’ expectations” (Draper, 2002). If the outcomes of the active drug are superior to that of the sham drug, then such a drug may be utilised in clinical practice (Sood, 2008). The most important component of the placebo effect is participant blindness to the different interventions (Shaik, 2008).

2.13.3 Similarities and Differences between the Hawthorne and Placebo Effects

Both the Hawthorne and placebo effects cause a psychological effect on the participants especially with respect to their reactions and perceptions (Sood, 2008). The principle difference between the two effects is that essentially the Hawthorne effect determines the participants’ response to their being studied while the placebo effect brings out their response to their belief in the treatment or intervention (Draper, 2002). In both effects there may be some deception on the part of the researcher with regards to the intervention. This is more applicable to the placebo effect (than the Hawthorne effect) where the researcher emphasizes the efficacy of the intervention (Draper, 2002).

2.13.4 Studies that have Utilised Sham Ultrasound as a Placebo

Sham or detuned ultrasound has been used as a placebo intervention in several recent studies as shown in Table 2.3.

Table 2.3 A summary of the recent studies that have utilised sham ultrasound as a placebo

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample/Population</th>
<th>Method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ter Riet et al. (1995)</td>
<td>88 pts with stage II decubitus ulcers</td>
<td>Active or sham U/S Rx 5 times a week over 12 weeks</td>
<td>No significant improvement with active or sham U/S</td>
</tr>
<tr>
<td>Pikula (1999)</td>
<td>36 pts with unilateral neck pain randomly allocated into 3 groups</td>
<td>Two groups: cervical SMT; placebo: sham U/S</td>
<td>↓ pain and ↑ cervical ROM SMT group (ipsilateral) compared to sham U/S</td>
</tr>
<tr>
<td>Rowlands and Brantingham (1999)</td>
<td>30 pts with patellofemoral pain syndrome</td>
<td>Group A: patellar mobilization Group B: sham U/S</td>
<td>Mobilisation of the knee was superior to sham U/S</td>
</tr>
<tr>
<td>Pellow and Brantingham (2001)</td>
<td>30 pts with subacute and chronic grade I and grade II ankle inversion sprains</td>
<td>Rx group: ankle SMT Placebo group: 5 min of sham U/S</td>
<td>Significant pain reduction, ↑ ankle ROM and function in Rx group compared to sham U/S (p &lt; 0.05)</td>
</tr>
<tr>
<td>Schiller (2001)</td>
<td>30 pts with thoracic pain</td>
<td>Rx group: thoracic SMT Control group: sham U/S</td>
<td>SMT was superior to sham U/S</td>
</tr>
<tr>
<td>Pillay (2003)</td>
<td>60 pts with upper trapezius TPs</td>
<td>Group 1: continuous U/S; Group 2: pulse U/S; Group 3: sham U/S</td>
<td>Both forms of active U/S was found to be more effective than sham U/S</td>
</tr>
</tbody>
</table>

*pts = patients; Rx = treatment; SMT = Spinal manipulative therapy; ROM = range of motion; U/S = ultrasound; ↑ = increase; ↓ = decrease; TPs = myofascial trigger points*
In most of the studies the experimental effect was significantly greater than the placebo effect of the sham ultrasound (Table 2.3). Physical therapeutic interventions such as spinal and extremity manipulation or mobilization were found to be superior to that of placebo with respect to decreasing pain and increasing function (Pikula, 1999; Rowlands and Brantingham, 1999; Pellow and Brantingham, 2001; Schiller, 2001; Table 2.3). When the effects of active ultrasound were compared to those of sham ultrasound, dissimilar results were observed in the studies of Ter Riet et al. (1995) and Pillay (2003) (Table 2.3). It is possible that decubitus ulcers (Ter Riet et al., 1995), which are difficult to treat, do not respond to the effects of ultrasound, but myofascial trigger points (Pillay, 2003) do as Ecternach (1965), Dyson et al. (1968), McDiarmid and Burns (1987), Dyson (1989), Dyson (1990), Pilla et al. (1990) and Ziskin et al. (1990) had shown that therapeutic ultrasound was useful in soft tissue healing and repair, scar tissue and joint contracture, chronic inflammations, bone healing and pain reduction.

2.14 CONCLUSION
Understanding the effect that therapeutic ultrasound has on blood flow is useful and helpful to the clinician in terms of selecting treatment protocols. Numerous contradictory results and conclusions have been drawn from many studies. Ultrasound is a modality that’s constantly used in practice and having knowledge about its effects would help in increasing its effectiveness.
CHAPTER THREE

METHODOLOGY

3.1 STUDY DESIGN
This research study was designed in the form of a double-blinded, placebo-controlled investigation using healthy asymptomatic individuals between the ages of 18-45 years. Ethical clearance for this study was obtained from The Faculty of Health Sciences Research Committee (Durban University of Technology; Certificate Number: FHSEC 001/07) (Appendix A).

3.2 ADVERTISING
Advertisements were placed on the notice boards of the Chiropractic Day Clinic (CDC), around the Durban University of Technology (DUT) Berea and City campuses, a local university, local libraries and shopping complexes. Prospective subjects were requested to contact the researcher telephonically for more information.

3.3 SAMPLE SIZE
A non-probability, convenience sampling technique was used in this study. A sample size of 50 healthy asymptomatic subjects (Esterhuizen, 2008) between the ages of 18-45 years was obtained. The age range of the subjects in this study was similar to those of Robinson and Buono (1995) and Noble et al. (2007). The total sample size of 50 subjects achieved a 91% power to detect the difference (Esterhuizen, 2008). Prospective subjects who responded personally or telephonically to the advertisements were provided with further information regarding the nature of the study. Thereafter, those who wished to participate in the study were invited for a consultation at the CDC. The subjects were told to refrain from part-taking in any alcohol, caffeine-containing products, medication and participating in exercise for at least 24 hours prior to their appointment.

All prospective subjects who contacted the researcher telephonically were asked the following questions:
1. “How old are you?”
2. “Are you a smoker?”
3. “Do you suffer from heart disease, diabetes or hypertension or any other blood vessel disease?”
4. “Are you currently on any medication?”
If the prospective subject was outside the age range of 18-45 years or answered “yes” to questions 2, 3 and 4, he/she was excluded.

3.4. INCLUSION AND EXCLUSION CRITERIA

3.4.1 Inclusion Criteria
- Healthy, asymptomatic individuals between the ages of 18-45 years.

3.4.2 Exclusion Criteria
- Smokers (Kool et al., 1993)
- History of cardiovascular and/or peripheral vascular disease and/or diabetes (Fabrizio et al., 1996; Noble et al., 2007)
- Injury to the neck or dominant arm (Fabrizio et al., 1996)
- Vascular abnormalities (venous thrombosis, emboli, bleeding disorders, etc.) (Noble et al., 2007)
- Alcohol intake (Noble et al., 2007)
- Caffeine intake (Noble et al., 2007)
- Participation in exercise (e.g. jogging or cycling) less than 24 hours prior to the therapeutic or sham ultrasound application (Noble et al., 2007)

3.5 PROCEDURE

3.5.1 Phase One
The subject presented to the CDC for his/her scheduled appointment. The researcher gave the subject a letter of information (Appendix B) to read and a verbal explanation of the study protocol was also given to the subject. The researcher responded to any questions that the subject may have had. If the subject agreed to participate in the study, he/she was required to sign an informed consent form (Appendix C). Each subject then underwent a case history (Appendix D) and a physical examination which also included a wrist and hand examination (Appendix E).

The subject was then randomly allocated to one of five groups (Table 3.1) by drawing a piece of paper with the letters “A” or “B” or “C” or “D” or “E” from an envelope. This procedure was done by a senior chiropractic intern who also recorded the grouping on a separate sheet (Appendix F). Appendix F was then handed to the CDC receptionist who filed it. The senior chiropractic intern and CDC receptionist were instructed not to reveal the grouping of the subject to the researcher, the subject or ultrasonographer. Appendix F was only handed to the researcher after completion of all 50 subjects for the unblinding procedure. The five intervention groups are shown in Table 3.1.
Table 3.1 The five intervention groups

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of subjects</th>
<th>Continuous TU/S</th>
<th>Pulse TU/S</th>
<th>ShamTU/S</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>10</td>
<td>0.2 W.cm(^2) *</td>
<td>-</td>
<td></td>
<td>5 minutes</td>
</tr>
<tr>
<td>B</td>
<td>10</td>
<td>0.2 W.cm(^2) *</td>
<td>0.2 W.cm(^2)</td>
<td></td>
<td>5 minutes</td>
</tr>
<tr>
<td>C</td>
<td>10</td>
<td>1.5 W.cm(^2) *</td>
<td>1.5 W.cm(^2)</td>
<td></td>
<td>5 minutes</td>
</tr>
<tr>
<td>D</td>
<td>10</td>
<td>1.5 W.cm(^2) *</td>
<td>0 W.cm(^2)</td>
<td></td>
<td>5 minutes</td>
</tr>
</tbody>
</table>

The dosage of 0.2 W.cm\(^2\) was based on similar intensities used by Dyson et al. (1976) while the dosage of 1.5 W.cm\(^2\) was based on the study of Robinson and Buono (1995).

TU/S = therapeutic ultrasound; No. = number

Thereafter, an appointment was made for the Doppler ultrasound evaluation at the Radiography Clinic (DUT) for the next phase of the study (within three days of the first consultation at the CDC). If time allowed, the ultrasound evaluation was also done after the completion of the case history and physical examination. Subjects who were to return for their Doppler ultrasound appointment were instructed to abstain from taking medication, alcohol/caffeine and undertaking exercise during the 24-hour period preceding the Doppler ultrasound evaluation (Noble et al., 2007). The importance of punctuality was also stressed by the researcher.

3.5.2 Phase Two

The subject presented at the Radiography Clinic on the specified appointment date and time (or after the completion of the case history and physical examination). The researcher enquired from the subject whether he/she had sustained any injury to the neck or dominant arm or if he/she had taken any medication (e.g. paracetamol for a headache) or if he/she had consumed any alcohol or caffeine or participated in exercise less than 24 hours prior to the appointment. If the subject answered “yes” to any of those questions, he/she was excluded. The researcher then introduced the subject to the ultrasonographer from the Department of Radiography.

**Preparation of the subject:** The subject was required to sit in a relaxed manner for five minutes to acclimatize to the laboratory environment whose room temperature was at a constant 23.5°C. The subject’s dominant arm was exposed and rested on the patient couch. An area 12 cm from the distal wrist crease was lightly demarcated on the ventral aspect of the forearm using a skin-marking pencil; this was the area of the therapeutic or sham ultrasound application. A senior chiropractic intern, after having inspected the subject’s grouping in Appendix F, set the therapeutic ultrasound unit intensity and the time to six minutes. A beeping sound is usually heard signaling that the time limit has been reached. This sound, however, would not have been heard if the unit was not switched on for the sham intervention. Therefore, the senior chiropractic intern utilised a stopwatch from the commencement of the ultrasound application and switched the unit off.
after five minutes. A piece of opaque cardboard was placed over the liquid crystal display (LCD) to prevent the researcher and the ultrasonographer from knowing the ultrasound settings (the double-blinding procedure).

**Baseline measurements:** A small amount of water-based ultrasound gel was applied to the application area. Baseline radial artery blood flow (m.s⁻¹) and radial artery lumen diameter (mm) were recorded using a 14 MHz musculoskeletal probe two-dimensional (2-D) Doppler ultrasound (Sonoline Sienna, Siemans Medical Division, Germany).

**Experiment and post-therapeutic ultrasound measurements:** The one MHz therapeutic ultrasound unit (Dynatron 850 plus, Dynatronics, Utah, USA) was set up as described above by the senior chiropractic intern. The timing on the stopwatch commenced at this point by the senior chiropractic intern. The researcher then administered the therapeutic ultrasound sweeping over the entire application area. After four minutes of application the therapeutic ultrasound head was moved away from the distal wrist area to allow for another set of blood flow and arterial lumen diameter measurements to be recorded. After a further minute, the senior chiropractic intern switched-off the therapeutic ultrasound unit. One-minute later, the post-therapeutic or sham ultrasound blood flow and arterial lumen diameter measurements were re-recorded. The total time for the therapeutic/sham ultrasound application was five minutes which was in keeping with the studies of Robinson and Buono (1995) and Noble et al. (2007).

The ultrasound gel was then wiped-off with disposable tissue paper. The results of the Doppler ultrasound measurements were then given to the subject. The researcher thanked the subject for participating in the study. This ended the subject's participation in the study. The Doppler and therapeutic/sham ultrasound procedure is summarised in **Figure 3.1**.

![Figure 3.1: Timeline of the experiment](image)

**Key:**
- **B** = Baseline Doppler ultrasound reading
- **U/S** = Therapeutic or sham ultrasound
- **D/S** = Doppler ultrasound reading during therapeutic or sham ultrasound application
- **D/SA** = Doppler ultrasound reading after therapeutic ultrasound or sham application
- **min** = minute(s)
3.6 ETHICAL CONSIDERATIONS IN THIS STUDY

Only healthy individuals with no medical conditions were included in this study. All subjects were thoroughly screened for contraindications to therapeutic ultrasound before inclusion in this study. An informed consent form was signed by all subjects in this study. Since all subjects were healthy, asymptomatic individuals, it was anticipated that there would be no adverse consequences for the subjects in any of the intervention groups (Clemente et al., 1992; Fabrizio et al., 1996; Ware et al., 2001; Noble et al., 2007). All subjects were informed that there was a one in five chance (i.e. 20%) of them receiving a sham “therapeutic” ultrasound.

3.7 STATISTICAL ANALYSIS

SPSS version 15.0 (SPSS Inc., Chicago, Illinois, USA) was used to analyse the data. A p-value <0.05 was considered statistically significant. One-way ANOVA was used to compare mean age, systolic and diastolic blood pressure between the five groups. Repeated measures ANOVA testing was used to assess intra-group changes in mean radial artery blood flow and radial artery lumen diameter values over time. Repeated measures ANOVA was also used to assess inter-group changes over time. A significant time group effect indicated a significant intervention effect (Esterhuizen, 2008). Pearson’s correlation analysis was used to examine intra-group and overall relationships between radial artery blood flow and radial artery lumen diameter at each time point.
CHAPTER FOUR

RESULTS

4.1 DEMOGRAPHIC DATA
The mean (± SD) age, systolic blood pressure and diastolic blood pressure of the subjects who participated in this study is shown in Table 4.1. The age of the subjects ranged from 18 to 38 years, the systolic blood pressure ranged from 96 to 138 mmHg and the diastolic blood pressure ranged from 56 to 82 mmHg. There was no significant difference between the mean (± SD) between the groups with respect to age (p = 0.341; one-way ANOVA), systolic (p = 0.797; one-way ANOVA) and diastolic blood pressure (p = 0.163; one-way ANOVA). The percentage of females compared to males that participated in this study is shown in Figure 4.1.

Table 4.1 Mean ± SD age, systolic and diastolic blood pressures of the subjects (n = 50) who participated in this study

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Systolic BP (mmHg)</th>
<th>Diastolic BP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (± SD)</td>
<td>21.4 (± 3.6)</td>
<td>111.6 (± 10.6)</td>
</tr>
</tbody>
</table>

BP = blood pressure

Figure 4.1 Gender percentage of the subjects (n = 50) who participated in this study
4.2 INTRA-GROUP ANALYSIS

4.2.1 Radial Artery Blood Flow

The mean (± SD) values for blood flow measured at baseline, during the therapeutic or sham ultrasound application and post-therapeutic or post-sham ultrasound application in each of the five intervention groups are shown in Table 4.2. There was no significant change in blood flow over time in any individual group or overall (p > 0.05; repeated measures ANOVA) (Table 4.2).

Table 4.2 Intra-group and overall changes in radial artery blood flow over time

<table>
<thead>
<tr>
<th>Group</th>
<th>Base BF (m.s⁻¹)</th>
<th>BF during (m.s⁻¹)</th>
<th>BF after (m.s⁻¹)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Mean</td>
<td>0.187</td>
<td>0.193</td>
<td>0.179</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>0.073</td>
<td>0.070</td>
<td>0.073</td>
</tr>
<tr>
<td>B</td>
<td>Mean</td>
<td>0.196</td>
<td>0.187</td>
<td>0.195</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>0.049</td>
<td>0.067</td>
<td>0.041</td>
</tr>
<tr>
<td>C</td>
<td>Mean</td>
<td>0.188</td>
<td>0.225</td>
<td>0.186</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>0.071</td>
<td>0.088</td>
<td>0.071</td>
</tr>
<tr>
<td>D</td>
<td>Mean</td>
<td>0.188</td>
<td>0.215</td>
<td>0.200</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>0.046</td>
<td>0.080</td>
<td>0.081</td>
</tr>
<tr>
<td>E</td>
<td>Mean</td>
<td>0.223</td>
<td>0.200</td>
<td>0.182</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>0.062</td>
<td>0.067</td>
<td>0.075</td>
</tr>
<tr>
<td>Total</td>
<td>Mean</td>
<td>0.197</td>
<td>0.204</td>
<td>0.189</td>
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<tr>
<td></td>
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<td>50</td>
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</tr>
<tr>
<td></td>
<td>SD</td>
<td>0.060</td>
<td>0.073</td>
<td>0.067</td>
</tr>
</tbody>
</table>

BF = blood flow; Base BF = baseline blood flow; BF during = blood flow measurements during therapeutic or sham ultrasound application; BF after = blood flow measurements after therapeutic or sham ultrasound application

4.2.2 Radial Artery Lumen Diameter

The mean (± SD) values for the radial artery lumen diameter measured at baseline, during the therapeutic or sham ultrasound application and post-therapeutic or post-sham ultrasound application in each of the five intervention groups are shown in Table 4.3. There was no significant change in the lumen diameter over time in any individual group or overall (p > 0.05; repeated measures ANOVA) (Table 4.3). The mean (± SD) radial artery lumen diameter in males was 2.5 mm (± 0.7) and 2.3 mm (± 0.4) in females.
Table 4.3 Intra-group and overall changes in radial artery lumen diameter over time

<table>
<thead>
<tr>
<th>Group</th>
<th>Base ALD (mm)</th>
<th>ALD during (mm)</th>
<th>ALD after (mm)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Mean 2.3</td>
<td>2.2</td>
<td>2.2</td>
<td>0.817</td>
</tr>
<tr>
<td></td>
<td>n 10</td>
<td>10</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD 0.4</td>
<td>0.5</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>Mean 2.4</td>
<td>2.4</td>
<td>2.3</td>
<td>0.893</td>
</tr>
<tr>
<td></td>
<td>n 10</td>
<td>10</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD 0.5</td>
<td>0.4</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Mean 2.5</td>
<td>2.4</td>
<td>2.7</td>
<td>0.054</td>
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<tr>
<td></td>
<td>n 10</td>
<td>10</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD 0.7</td>
<td>0.7</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>Mean 2.5</td>
<td>2.4</td>
<td>2.4</td>
<td>0.883</td>
</tr>
<tr>
<td></td>
<td>n 10</td>
<td>10</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD 0.5</td>
<td>0.8</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>Mean 2.5</td>
<td>2.5</td>
<td>2.3</td>
<td>0.471</td>
</tr>
<tr>
<td></td>
<td>n 10</td>
<td>10</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD 0.8</td>
<td>0.7</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>Mean 2.4</td>
<td>2.4</td>
<td>2.4</td>
<td>0.615</td>
</tr>
<tr>
<td></td>
<td>n 50</td>
<td>50</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD 0.6</td>
<td>0.6</td>
<td>0.6</td>
<td></td>
</tr>
</tbody>
</table>

Base ALD = baseline radial artery lumen diameter measurements; ALD during = radial artery lumen diameter measurements during the therapeutic or sham ultrasound application; ALD after = radial artery lumen diameter measurements after the therapeutic or sham ultrasound application

4.3 INTER-GROUP ANALYSIS

4.3.1 Radial Artery Blood Flow

There was no statistically significant intervention effect ($p = 0.359$; repeated measures ANOVA) (Table 4.4) for radial artery blood flow. The rate of change of blood flow was not significantly different ($p > 0.05$, repeated measures ANOVA) between the five intervention groups.

Table 4.4 Repeated measures ANOVA for radial artery blood flow between groups

<table>
<thead>
<tr>
<th>Effect</th>
<th>Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>Wilk’s lambda = 0.949</td>
<td>0.315</td>
</tr>
<tr>
<td>Time group</td>
<td>Wilk’s lambda = 0.824</td>
<td>0.359</td>
</tr>
<tr>
<td>Group</td>
<td>$F = 0.131$</td>
<td>0.970</td>
</tr>
</tbody>
</table>
4.3.2 Radial Artery Lumen Diameter
There was no statistically significant intervention effect ($p = 0.698$; repeated measures ANOVA) for the radial artery lumen diameter as shown in Table 4.5, meaning that the rate of change over time between the groups was not significantly different.

Table 4.5 Repeated measures ANOVA for radial artery lumen diameter between groups

<table>
<thead>
<tr>
<th>Effect</th>
<th>Statistic</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>Wilk’s lambda = 0.980</td>
<td>0.639</td>
</tr>
<tr>
<td>Time group</td>
<td>Wilk’s lambda = 0.885</td>
<td>0.698</td>
</tr>
<tr>
<td>Group</td>
<td>$F = 0.364$</td>
<td>0.833</td>
</tr>
</tbody>
</table>

4.4 CORRELATION ANALYSIS

4.4.1 Baseline
There was an overall weak positive correlation between radial artery blood flow and radial artery lumen diameter ($r = 0.508$; Pearson’s correlation; $n = 100$; Figure 4.2).

![Figure 4.2](image)

**Figure 4.2** Pearson’s correlation between baseline radial artery blood flow and radial artery lumen diameter in all groups combined ($n = 100$)

4.4.2 During the Therapeutic or Sham Ultrasound Application
During the therapeutic or sham ultrasound application there was an overall weak positive correlation between radial artery blood flow and radial artery lumen diameter ($r = 0.541$; Pearson’s correlation; $n = 100$; Figure 4.3).
4.4.3 Post-Therapeutic or Post-Sham Ultrasound Application

After the therapeutic or sham ultrasound application there was an overall weak positive correlation between radial artery blood flow and radial artery lumen diameter ($r = 0.532$; Pearson's correlation; $n = 100$; Figure 4.4).

4.4.4 Pearson's Correlation between Baseline Radial Artery Blood Flow and Radial Artery Lumen Diameter in All Five Groups

There was a weak to moderate positive correlation between baseline radial artery blood flow and radial artery lumen diameter in the five intervention groups as shown in Table 4.6.
Table 4.6 Pearson’s correlation between baseline radial artery blood flow and radial artery lumen diameter in all five groups

<table>
<thead>
<tr>
<th>Base BF A</th>
<th>Base diameter A</th>
<th>Base BF B</th>
<th>Base diameter B</th>
<th>Base BF C</th>
<th>Base diameter C</th>
<th>Base BF D</th>
<th>Base diameter D</th>
<th>Base BF E</th>
<th>Base diameter E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base BF and base diameter</td>
<td>PC</td>
<td>1</td>
<td>0.558</td>
<td>1</td>
<td>0.283</td>
<td>1</td>
<td>0.687</td>
<td>1</td>
<td>0.484</td>
</tr>
<tr>
<td>n</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

 Baseline BF = baseline blood flow; Base diameter = baseline radial artery lumen diameter; PC = Pearson’s correlation
 A = continuous ultrasound at 0.2 W.cm⁻²; B = pulse ultrasound at 0.2 W.cm⁻²; C = continuous ultrasound at 1.5 W.cm⁻²; D = pulse ultrasound at 1.5 W.cm⁻²; E = sham ultrasound at 0 W.cm⁻²

4.4.5 Pearson’s Correlation between Radial Artery Blood Flow and Radial Artery Lumen Diameter during Intervention in All Five Groups

There was a weak to moderate positive correlation between radial artery blood flow and radial artery lumen diameter during intervention in the five intervention groups as shown in Table 4.7.

Table 4.7 Pearson’s correlation between radial artery blood flow and radial artery lumen diameter during intervention in all five groups

<table>
<thead>
<tr>
<th>BF during A</th>
<th>Diameter during A</th>
<th>BF during B</th>
<th>Diameter during B</th>
<th>BF during C</th>
<th>Diameter during C</th>
<th>BF during D</th>
<th>Diameter during D</th>
<th>BF during E</th>
<th>Diameter during E</th>
</tr>
</thead>
<tbody>
<tr>
<td>BF and diameter during</td>
<td>PC</td>
<td>1</td>
<td>0.458</td>
<td>1</td>
<td>0.052</td>
<td>1</td>
<td>0.678</td>
<td>1</td>
<td>0.669</td>
</tr>
<tr>
<td>n</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

 BF during = blood flow during therapeutic or sham ultrasound application; Diameter during = radial artery lumen diameter during therapeutic or sham ultrasound application; PC = Pearson’s correlation
 A = continuous ultrasound at 0.2 W.cm⁻²; B = pulse ultrasound at 0.2 W.cm⁻²; C = continuous ultrasound at 1.5 W.cm⁻²; D = pulse ultrasound at 1.5 W.cm⁻²; E = sham ultrasound at 0 W.cm⁻²

4.4.6 Pearson’s Correlation between Radial Artery Blood Flow and Radial Artery Lumen Diameter Post-intervention in All Five Groups

The correlation between radial artery blood flow and radial artery lumen diameter post-intervention ranged from weak to moderate to strong as shown in Table 4.8.

Table 4.8 Pearson’s correlation between radial artery blood flow and radial artery lumen diameter post-intervention in all five groups

<table>
<thead>
<tr>
<th>Post-BF A</th>
<th>Post-diameter A</th>
<th>Post-BF B</th>
<th>Post-diameter B</th>
<th>Post-BF C</th>
<th>Post-diameter C</th>
<th>Post-BF D</th>
<th>Post-diameter D</th>
<th>Post-BF E</th>
<th>Post-diameter E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-BF and diameter</td>
<td>PC</td>
<td>1</td>
<td>0.629</td>
<td>1</td>
<td>0.093</td>
<td>1</td>
<td>0.890</td>
<td>1</td>
<td>0.365</td>
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<tr>
<td>n</td>
<td>10</td>
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<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

 Post-BF = post-therapeutic or post-sham ultrasound radial artery blood flow; Post diameter = post-therapeutic or post-sham radial artery lumen diameter ; PC = Pearson’s correlation
 A = continuous ultrasound at 0.2 W.cm⁻²; B = pulse ultrasound at 0.2 W.cm⁻²; C = continuous ultrasound at 1.5 W.cm⁻²; D = pulse ultrasound at 1.5 W.cm⁻²; E = sham ultrasound at 0 W.cm⁻²
CHAPTER FIVE

DISCUSSION

5.1 DEMOGRAPHIC DATA
All subjects who participated in this study were healthy asymptomatic individuals as were
the subjects in the studies of Bickford and Duff (1953), Robinson and Buono (1995),
Fabrizio et al. (1996), Ware et al. (2001) and Noble et al. (2007). There was a higher
number of males who participated in this study (Figure 4.1), which was similar to the
observations of Bickford and Duff (1953) and Ware et al. (2001). There were only male
subjects in the studies of Abramson et al. (1960) and Baker and Bell (1991) while
Clemente et al. (1992), Robinson and Buono (1995), Fabrizio et al. (1996) and Noble et
al. (2007) had an equal number of male and female subjects. None of the studies reported
significant differences in the results between the genders.

The age of the subjects ranged from 18 to 38 years which was similar to that of the
subjects in the studies of Abramson et al. (1960), Fabrizio et al. (1996) and Noble et al.
(2007). The mean age of the subjects (Table 4.1) was similar to that of the subjects in the
study by Baker and Bell (1991). The mean (± SD) and range (Table 4.1) of the systolic
and the diastolic blood pressures were within the limits of normal blood pressure (i.e. the
normotensive range) (Marieb, 2006). The higher systolic blood pressure observed in some
individuals (but still within the normal range) could be attributed to the “white coat
hypertension” syndrome (Ganong, 2001) where a transient increase in blood pressure
was due to the subject being nervous as a result of participating in a research project.

The temperature in the room in which the ultrasound was conducted was similar to that of
Abramson et al. (1960) and Baker and Bell (1991). This insured that were no variations in
environmental temperature that would have affected blood pressure and vasomotor
response in the blood vessels (Guyton and Hall, 2006).

5.2 RADIAL ARTERY BLOOD FLOW AND RADIAL ARTERY LUMEN DIAMETER
The mean (± SD) radial artery lumen diameter in this study was less than that reported by
Yoon (1998) and Yoo et al. (2005) (Table 2.1), but larger than that reported by Shima et
al. (1995) and Ku et al. (2006) (Table 2.1) and the same as that reported by Loh et al.
(2007) (Table 2.1). The mean (± SD) for radial artery lumen diameter of males was larger
than that of the females which was in agreement with the observations of Yoon (1998) and Yoo et al. (2005).

There was no significant change in radial artery blood flow or radial artery lumen diameter ($p > 0.05$) across the three time intervals within (Tables 4.2 and 4.3) or between the five intervention groups (Tables 4.4 and 4.5). The results of this study, therefore, supported the observations of Clemente et al. (1992) (Table 2.2), but were in contrast to those of Fabrizio et al. (1996) who reported an increase in blood flow in the popliteal artery following application of a one MHz ultrasound at intensities of 1.0 and 1.5 W.cm$^{-2}$ (Table 2.2). No direct comparisons were possible with the results of the other studies in Table 2.2 due to differences in the tissue where blood flow was measured, therapeutic ultrasound frequency and intensity settings and tools to measure the blood flow.

The lack of a penetrative effect of the pulse and continuous ultrasound at the two different intensities of 0.2 W.cm$^{-2}$ and 1.5 W.cm$^{-2}$ could also account for the results of this study as Bickford and Duff (1953) reported that increased blood flow in the forearm region was likely to occur with deep tissue penetration and Schwan et al. (1954) had reported that radiating techniques were effective only if the depth of penetration was sufficient. The thermogenic effects attributed to continuous (Baker et al., 2001) and pulse (MacDonald and Shipster, 1981; Sandler and Feingold, 1981; Williams, 1987) ultrasound did not occur as the region of the radial artery in the forearm was not sufficiently heated to result in increased blood flow. Kemp et al. (1948) observed that hyperemia in the limbs of dogs only occurred when there was a significant temperature increase. It could be that the cellular and muscular components of the radial artery wall (2.2) were not sufficiently heated following ultrasound application as Abramson et al. (1960) observed that temperature increases occurred markedly in bones and nerves following therapeutic ultrasound application. If heating did occur with ultrasound application, it was transient and easily lost to the environment especially if cutaneous vasodilation occurred (Bickford and Duff, 1953). Reid and Cummings (1973) had stated that the area of therapeutic ultrasound application was not to be greater than three times that of the ultrasound crystal. If the area of ultrasound application was large, cooling would occur as soon as the ultrasound head was moved away (Bickford and Duff, 1953). The area of ultrasound application in the study was probably too large and could also be a reason why no significant effect was observed (Tables 4.2 and 4.4). Robinson and Buono (1995) (Table 2.2) used the same explanation to account for a lack of significant findings with respect to a change in forearm blood flow following ultrasound application.
The microstreaming effect attributed to pulse ultrasound (Dyson, 1987; Ter Haar, 1987) had no significant effect ($p > 0.05$) on radial artery blood flow as there was no cell membrane damage in the arterial wall (Dyson, 1987). Since there was no influx of calcium, sodium and other ions and metabolites into the cellular components of the radial artery wall, there was no change in the tone of the vascular smooth muscle wall following pulse ultrasound application. If these ionic changes had occurred, then there would have been changes to the vascular smooth muscle tone (Chapman et al., 1979) which could have affected blood flow in the radial artery. Both pulse and continuous ultrasound application also did not result in the release of important vasodilators such as kinins, histamine and prostaglandins (Solomon et al., 1990; Guyton and Hall, 2006).

The lack of consistent strong correlation results (Figures 4.2, 4.3 and 4.4; Tables 4.6, 4.7 and 4.8) of an association between changes in the radial artery lumen diameter and radial artery blood flow during or following therapeutic or sham ultrasound application is not surprising as according to Poiseuille’s Law (2.9), the flow ($Q$) in a vessel is proportional to the radius ($r$) to the fourth power (Davidovits, 2007) as shown below:

$$Q \propto \frac{1}{r^4}$$

Since the length of the radial artery and viscosity did not change, blood flow changes did not occur since the arterial lumen diameter (which is twice the radius) did not significantly change during or after the pulse, continuous therapeutic or sham ultrasound intervention.

The sham ultrasound application in this study had no significant effect ($p > 0.05$) on radial artery blood flow or arterial lumen diameter. The massaging effect attributed to sham ultrasound (Fabrizio et al., 1996; Noble et al., 2007) was not sufficient enough to result in a significant change in blood flow in the radial artery. The Hawthorne effect (Mouton and Marais, 1994) was equally applicable to all the subjects who participated in this study as all the subjects were aware that they were being observed by the researcher, ultrasonographer and senior chiropractic intern. The impact of the Hawthorne effect was not quantifiable in this study since the increased clinical surveillance was applicable to all subjects in the five groups. Furthermore, no specific or different instructions were given to the subjects in any of the groups. This was also a contributory factor for a lack of the Hawthorne effect as De Amici et al. (2000) and McCarney et al. (2007) observed that instructions given to participants in clinical trials contributed to the clinical significance of the Hawthorne effect.
All subjects were also informed that there was a 20% chance of their receiving sham ultrasound. Since there was no perceptible difference in sensation during active (continuous and pulse) and sham ultrasound application, the placebo effect (Draper, 2002) was also applicable to all subjects. The results of this study were similar to those of Ter Riet et al. (1995) (Table 2.3) who showed that active or sham ultrasound had no significant effect on the healing of decubitus ulcers, but were in contrast to Pillay (2003) (Table 2.3) who showed that active ultrasound was superior to sham ultrasound in the treatment of myofascial trigger points. A possible explanation for this observation could be that striated (voluntary) muscle tissue may respond differently to the effects of therapeutic ultrasound than the smooth muscle of arteries.
CHAPTER SIX

CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSION

The primary aims of the study were:

- To determine the effect of therapeutic or sham ultrasound on radial artery blood flow (m.s\(^{-1}\))
- To determine the effect of therapeutic or sham ultrasound on radial artery lumen diameter (mm)

With regards to the aims of this study, the results of this study showed that continuous, pulse ultrasound or sham ultrasound had no significant effect on radial artery blood flow and radial artery lumen diameter. Furthermore, active ultrasound (continuous and pulse) was not superior to sham ultrasound in significantly affecting blood flow in a muscular artery.

In terms of the associated hypotheses that were set at the onset of the study:

The Null Hypothesis (H\(_0\)) which stated there would be no significant association between pulse, continuous or sham ultrasound and radial artery blood flow was accepted.

The Null Hypothesis (H\(_0\)) which stated there would be no significant association between pulse, continuous or sham ultrasound and radial artery lumen diameter was accepted.

The Null Hypothesis (H\(_0\)) which stated there would be no significant association between the radial artery blood flow and radial artery lumen diameter was accepted.

6.1 RECOMMENDATION

Recommendations for future studies include the following investigation:

- An animal study to determine the effect of ultrasound on blood flow in damaged blood vessels.
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Varatharajullu, D. (desireevara@yahoo.com), 19 March 2008. *Statistical analysis*. Email to T. Esterhuizen. (esterhuizent@ukzn.ac.za).


## APPENDIX A

### ETHICS CLEARANCE CERTIFICATE

<table>
<thead>
<tr>
<th>Student Name</th>
<th>DEGREE VARKHALAVI</th>
</tr>
</thead>
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<tr>
<td>Ethics Reference No.</td>
<td>FHSEC</td>
</tr>
<tr>
<td>Date of FRC Approval</td>
<td>12/05/08</td>
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<tr>
<td>Student No.</td>
<td>20100732</td>
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</tbody>
</table>

**Research Title:**
A DOUBLE-BLIND PLACER CONTROLLED INVESTIGATION INTO THE EFFECT OF THERAPEUTIC ULTRASOUND ON RANAL ARTERY BLOOD FLOW.

In terms of the ethical considerations for the conduct of research in the Faculty of Health Sciences, Durban University of Technology, this proposal meets with institutional requirements and confirms the following ethical obligations:

1. The researcher has read and understood the research ethics policy and procedures as endorsed by the Durban University of Technology, has sufficiently answered all questions pertaining to ethics in the DUT-186 and agrees to comply with them.
2. The researcher will report any serious adverse events pertaining to the research to the Faculty of Health Sciences Research Ethics Committee.
3. The researcher will submit any major additions or changes to the research proposal after approval has been granted to the Faculty of Health Sciences Research Committee for consideration.
4. The researcher, with the supervisor and co-researchers will take full responsibility in ensuring that the protocol is adhered to.
5. The following section must be completed if the research involves human participants:

<table>
<thead>
<tr>
<th>Requirement</th>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provision has been made to obtain informed consent of the participants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potential psychological and physical risks have been considered and minimised</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Provision has been made to avoid undue intrusion with regard to participants and community</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Rights of participants will be safeguarded in relation to: Measures for the protection of anonymity and the maintenance of confidentiality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Access to research information and findings.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>- Termination of involvement without compromise</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>- Misleading promises regarding benefits of the research</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Signature of Student/Researcher:**

**Date:** 28/05/08

**Signature of Supervisor(s):**

**Date:** 2 June 2008

**Signature of Head of Department:**

**Date:** 3 June 2008

**Signature: Chairperson of Research Ethics Committee:**

**Date:** 2 June 2008
APPENDIX B

LETTER OF INFORMATION

Date:

Dear Participant, welcome to my research project.

Title of Research: A double-blinded placebo controlled investigation into the effect of therapeutic ultrasound on radial artery blood flow

Name of student: Desiree Varatharajullu, Contact number: 0782220942/ 373 2205

Name of supervisor: Dr. J. Shaik (M. Tech. Chiro.; M. Med. Sci. (SM), Contact number: (031) 373 2588

You have been selected to take part in a study investigating the effect of therapeutic ultrasound on radial artery blood flow and luminal (the hollow area of the blood vessel through which blood flows) diameter by means of Doppler ultrasonography (a device that measure blood flow by means of sound waves) in healthy people

Fifty people will be required to complete this study.

To be part of this study you must
- Be healthy with no symptoms and between the ages of 18-45 years

You will not be eligible to take part in this study if you
- Are a smoker
- Have any disease of the heart, blood vessels or diabetes
- Have any injury to the neck or your dominant arm
- Have any bleeding diseases
- Have taken any alcohol/caffeine-containing products or medication or exercise (e.g. jogging or cycling) less than 24 hours before the ultrasound application

Research process:
At the first consultation you will read this information sheet and ask any questions about the research. If you agree to take part in this research, you will have to sign an informed consent form. Then, the researcher will take a case history and a physical examination will be done. You will then be assigned to one of five therapeutic ultrasound groups. Please note that one of the groups is a sham ultrasound (i.e. the unit will not be switched on). However, neither the researcher, ultrasonographer (the person who will be doing the actual Doppler ultrasound) nor you will know which group you have been assigned to. You are not expected to feel anything during the ultrasound application (active or the sham one), with exception of the ultrasound gel and metal head of the ultrasound probe. Depending on the availability of the ultrasonographer, the Doppler ultrasound evaluation will be done on the same day after this appointment or within 3 working days. Please do not take any alcohol, caffeine-containing products and medication or take part in any exercise for at least 24 hours before your second appointment. Please arrive at least 10 minutes before your second appointment.

Risks and discomfort:
There are no risks or discomforts to you

Remuneration and costs:
You will not be offered any form of remuneration for taking part in the study. The initial consultation and the Doppler ultrasound evaluation are free of charge.

Implications for withdrawal from the research:
You are free to withdraw at any stage without any negative repercussions.

Benefits of the study:
This study will help in determining how healing occurs following ultrasound application.
Confidentiality and ethics
All your medical records will be kept confidential and will be stored in the Chiropractic Day Clinic for 5 years, after which it will be shredded. Your name will not appear on any of the data sheets or thesis.

Please don’t hesitate to ask questions on any aspect of this study. Should you have any complaints or queries, please do not hesitate to contact my research supervisor at the above details or the Head of the Faculty of Health Sciences Research Committee, Prof. N. Gwele on (031) 373 2704.

Thank you.
Yours sincerely,

Desiree Varatharajullu (Research student)  Dr J. Shaik (Supervisor)
APPENDIX C

INFORMED CONSENT FORM

Date: 

Title of research project: A double-blinded placebo controlled investigation into the effect of therapeutic ultrasound on radial artery blood flow

Name of supervisor: Dr. J. Shaik [M. Tech: Chiropractic; M. Med. Sci. (SM)]
Tel: (031) 373 2588

Name of research student: Desiree Varatharajullu
Tel: (031) 373 2205 / 0782220942

Please circle the appropriate answer YES/NO

1. Have you read the research information sheet? Yes No
2. Have you had an opportunity to ask questions regarding this study? Yes No
3. Have you received satisfactory answers to your questions? Yes No
4. Have you had an opportunity to discuss this study? Yes No
5. Have you received enough information about this study? Yes No
6. Do you understand the implications of your involvement in this study? Yes No
7. Do you understand that you are free to withdraw from this study? Yes No
   ● at any time
   ● without having to give any a reason for withdrawing, and
   ● without affecting your future health care.
8. Do you agree to voluntarily participate in this study Yes No
9. Who have you spoken to? ________________________________

Please ensure that the researcher completes each section with you
If you have answered NO to any of the above, please obtain the necessary information before signing

Please print in block letters:

Patient/Subject Name: ________________________________ Signature: ________________________________

Witness Name: ________________________________ Signature: ________________________________
### APPENDIX D

**DURBAN UNIVERSITY OF TECHNOLOGY**

**CHIROPRACTIC DAY CLINIC**

**CASE HISTORY**

<table>
<thead>
<tr>
<th>Patient:</th>
<th>Date:</th>
<th>File #:</th>
<th>Age:</th>
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<table>
<thead>
<tr>
<th>Sex</th>
<th>Sex:</th>
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<table>
<thead>
<tr>
<th>Intern:</th>
<th>Intern:</th>
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</table>

**FOR CLINICIANS USE ONLY:**

Initial visit

Clinician: Signature:

**Case History:**

Examination:

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<th>Previous:</th>
<th>Current:</th>
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X-Ray Studies:

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Clinical Path. lab:

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<th>Previous:</th>
<th>Current:</th>
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**CASE STATUS:**

<table>
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<th>PTT:</th>
<th>Signature:</th>
<th>Date:</th>
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</thead>
</table>

**CONDITIONAL:**

Reason for Conditional:

Signature: Date:

Conditions met in Visit No: Signed into PTT: Date:

Case Summary signed off: Date:
### Intern’s Case History:

1. **Source of History:**

2. **Chief Complaint: (patient’s own words):**

3. **Present Illness:**

<table>
<thead>
<tr>
<th></th>
<th>Complaint 1</th>
<th>Complaint 2</th>
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<tbody>
<tr>
<td><strong>Location</strong></td>
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<tr>
<td><strong>Onset:</strong></td>
<td>Initial:</td>
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<tr>
<td></td>
<td>Recent:</td>
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<tr>
<td><strong>Cause:</strong></td>
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<tr>
<td><strong>Duration</strong></td>
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<td></td>
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<tr>
<td><strong>Frequency</strong></td>
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<td></td>
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<tr>
<td><strong>Pain (Character)</strong></td>
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<td></td>
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<tr>
<td><strong>Progression</strong></td>
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<td></td>
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<tr>
<td><strong>Aggravating Factors</strong></td>
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<tr>
<td><strong>Relieving Factors</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Associated S &amp; S</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Previous Occurrences</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Past Treatment</strong></td>
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<td></td>
</tr>
<tr>
<td><strong>Outcome:</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4. **Other Complaints:**

5. **Past Medical History:**

   - General Health Status
   - Childhood Illnesses
   - Adult Illnesses
   - Psychiatric Illnesses
   - Accidents/Injuries
   - Surgery
   - Hospitalizations
6. **Current health status and life-style:**

- Allergies
- Immunizations
- Screening Tests incl. x-rays
- Environmental Hazards (Home, School, Work)
- Exercise and Leisure
- Sleep Patterns
- Diet
- Current Medication
  - Analgesics/week:
  - Tobacco
- Alcohol
- Social Drugs

7. **Immediate Family Medical History:**

- Age
- Health
- Cause of Death
- DM
- Heart Disease
- TB
- Stroke
- Kidney Disease
- CA
- Arthritis
- Anaemia
- Headaches
- Thyroid Disease
- Epilepsy
- Mental Illness
- Alcoholism
- Drug Addiction
- Other

8. **Psychosocial history:**

- Home Situation and daily life
- Important experiences
- Religious Beliefs
9. **Review of Systems:**

- General
- Skin
- Head
- Eyes
- Ears
- Nose/Sinuses
- Mouth/Throat
- Neck
- Breasts
- Respiratory
- Cardiac
- Gastro-intestinal
- Urinary
- Genital
- Vascular
- Musculoskeletal
- Neurologic
- Haematologic
- Endocrine
- Psychiatric

8 Sept 2006
# PHYSICAL EXAMINATION

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<tr>
<th>Patient Name :</th>
<th>File no :</th>
<th>Date :</th>
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<tbody>
<tr>
<td>Student :</td>
<td>Signature :</td>
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## VITALS:

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<thead>
<tr>
<th>Pulse rate:</th>
<th>Respiratory rate:</th>
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<tr>
<td>Blood pressure:</td>
<td>R</td>
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<tr>
<td>Temperature:</td>
<td>Height:</td>
</tr>
<tr>
<td>Weight:</td>
<td>Any recent change? Y / N</td>
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<tr>
<td>If Yes: How much gain/loss</td>
<td>Over what period</td>
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## GENERAL EXAMINATION:

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<th>General Impression</th>
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<tr>
<td>Skin</td>
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<tr>
<td>Jaundice</td>
</tr>
<tr>
<td>Pallor</td>
</tr>
<tr>
<td>Clubbing</td>
</tr>
<tr>
<td>Cyanosis (Central/Peripheral)</td>
</tr>
<tr>
<td>Oedema</td>
</tr>
</tbody>
</table>

### Lymph nodes
- Head and neck
  - Axillary
  - Epitrochlear
  - Inguinal

### Pulses
- Urinalysis

## SYSTEM SPECIFIC EXAMINATION:

- CARDIOVASCULAR EXAMINATION
- RESPIRATORY EXAMINATION
- ABDOMINAL EXAMINATION
- NEUROLOGICAL EXAMINATION

## COMMENTS

Clinician: Signature :
**HAND AND WRIST REGIONAL EXAMINATION**

### Observation:

<table>
<thead>
<tr>
<th></th>
<th>Right</th>
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</thead>
<tbody>
<tr>
<td>1.</td>
<td>bony and soft tissue contours</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>hand posture</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>vasomotor changes</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>scars, skin creases, and muscle wasting</td>
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</tr>
<tr>
<td>5.</td>
<td>fingernails</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>dominant hand</td>
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### Palpation:

**Posterior surface**

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<tr>
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<tbody>
<tr>
<td>1.</td>
<td>Anatomical snuff box</td>
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<tr>
<td>2.</td>
<td>Carpal bones</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Metacarpal bones</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Phalanges</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Pulses and capillary refill</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Radial styloid</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Radial (Lister’s) tubercle</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>Ulnar styloid</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>6 extensor tendon tunnels</td>
<td></td>
</tr>
<tr>
<td>i.</td>
<td>Abd poll long</td>
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<tr>
<td></td>
<td>Ext poll brev</td>
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</tr>
<tr>
<td>ii.</td>
<td>ECRB</td>
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</tr>
<tr>
<td></td>
<td>ECRL</td>
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</tr>
<tr>
<td>iii.</td>
<td>Ext poll long</td>
<td></td>
</tr>
<tr>
<td>iv.</td>
<td>Ext digit</td>
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</tr>
<tr>
<td>v.</td>
<td>Ext digit mini</td>
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<td>vi.</td>
<td>ECU</td>
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**Anterior surface**

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<tr>
<td>1.</td>
<td>Tendons (Lat to med)</td>
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</tr>
<tr>
<td>a.</td>
<td>Flexor carpi radialis</td>
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</tr>
<tr>
<td>b.</td>
<td>Flexor poll longus</td>
<td></td>
</tr>
<tr>
<td>c.</td>
<td>Flexor digit super</td>
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</tr>
<tr>
<td>d.</td>
<td>Flexor digit profund</td>
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</tr>
<tr>
<td>e.</td>
<td>Palmaris long</td>
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</tr>
<tr>
<td>f.</td>
<td>Flexor carpi ulnaris</td>
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</tr>
<tr>
<td>2.</td>
<td>Palmar fascia and intrinsic muscles</td>
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### Active movements

<table>
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<tr>
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<tbody>
<tr>
<td>1.</td>
<td>Pronation (85-90°)</td>
<td>Tissue stretch</td>
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<tr>
<td>2.</td>
<td>Supination (85-90°)</td>
<td>Tissue stretch</td>
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<tr>
<td>3.</td>
<td>Ulnar deviation (15°)</td>
<td>Bone</td>
</tr>
<tr>
<td>4.</td>
<td>Radial deviation (30-45°)</td>
<td>Bone</td>
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<tr>
<td>5.</td>
<td>Wrist flexion (80-90°)</td>
<td>Tissue stretch</td>
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<tr>
<td>6.</td>
<td>Wrist extension (70-90°)</td>
<td>Tissue stretch</td>
</tr>
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<td>7.</td>
<td>Finger movements</td>
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<td>8.</td>
<td>Thumb movements</td>
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### Passive movements

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### Resisted isometric movements

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<tr>
<td>1. Flexion</td>
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<td></td>
</tr>
<tr>
<td>2. Extension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Radial dev</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Ulnar dev</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Finger</td>
<td>Opposition</td>
<td>Adduction</td>
</tr>
<tr>
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### Functional movements

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<thead>
<tr>
<th>Gross Grip Strength</th>
<th>Right</th>
<th>Left</th>
<th>Precision Grip Strength</th>
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<tbody>
<tr>
<td></td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>1. fist grip</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2. cylinder grip</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>3. hook grip</td>
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<td>4. sphere grip</td>
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### Special tests

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<td>3. Phalan's test</td>
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<td>4. Reverse phalan's test</td>
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<td>5. Allen's test</td>
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<td>6. Froment's sign</td>
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<tr>
<td>7. Watson's test</td>
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<tr>
<td>8. Scaphoid compression test</td>
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<tr>
<td>9. Lunatrotiquetal ballottment test</td>
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</tr>
<tr>
<td>10. Bunnel littler test</td>
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<tr>
<td>11. Tight retinacular test</td>
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<td>12. Ligament stability</td>
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### Joint play movements

**Hand and fingers**

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<tbody>
<tr>
<td>1. MCP and PIP + DIP</td>
<td>Long axis extension</td>
<td>AP, PA glide</td>
</tr>
<tr>
<td></td>
<td>Rotation</td>
<td>Side glide</td>
</tr>
<tr>
<td>2. Distal inter-metacarpals</td>
<td>AP, PA glide</td>
<td>Rotation</td>
</tr>
</tbody>
</table>

**Wrist**

<table>
<thead>
<tr>
<th></th>
<th>Right</th>
<th>Left</th>
</tr>
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<tbody>
<tr>
<td>1. Long axis extension</td>
<td></td>
<td></td>
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<tr>
<td>2. AP glide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Carpal extension</td>
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<td></td>
</tr>
<tr>
<td>4. Carpal flexion</td>
<td></td>
<td></td>
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<tr>
<td>5. Ulnar deviation</td>
<td></td>
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<tr>
<td>6. Radial deviation</td>
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<tr>
<td>7. Ul-men-triq AP+ PA glide</td>
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<tr>
<td>8. Inf rad-ulnar rotation</td>
<td>AP, PA glide</td>
<td>Rotation</td>
</tr>
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</table>
## APPENDIX F

### DATA SHEET

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
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<tbody>
<tr>
<td>Continuous ultrasound at 0.2 W.cm² for 5 minutes</td>
<td>Pulse ultrasound at 0.2 W.cm² for 5 minutes</td>
<td>Continuous ultrasound at 1.5 W.cm² for 5 minutes</td>
<td>Pulse ultrasound at 1.5 W.cm² for 5 minutes</td>
<td>Placebo ultrasound at 0 W.cm² for 5 minutes</td>
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