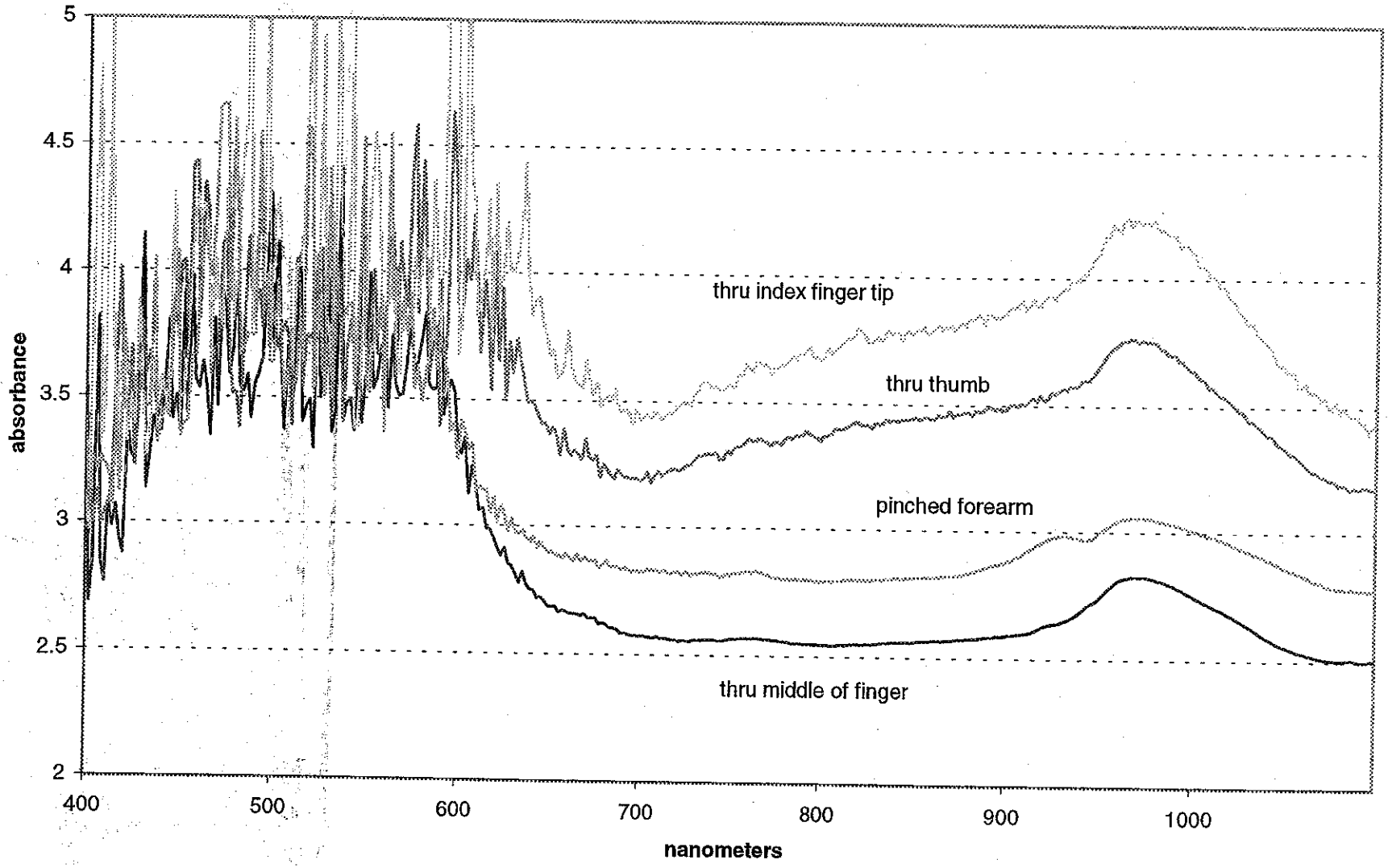
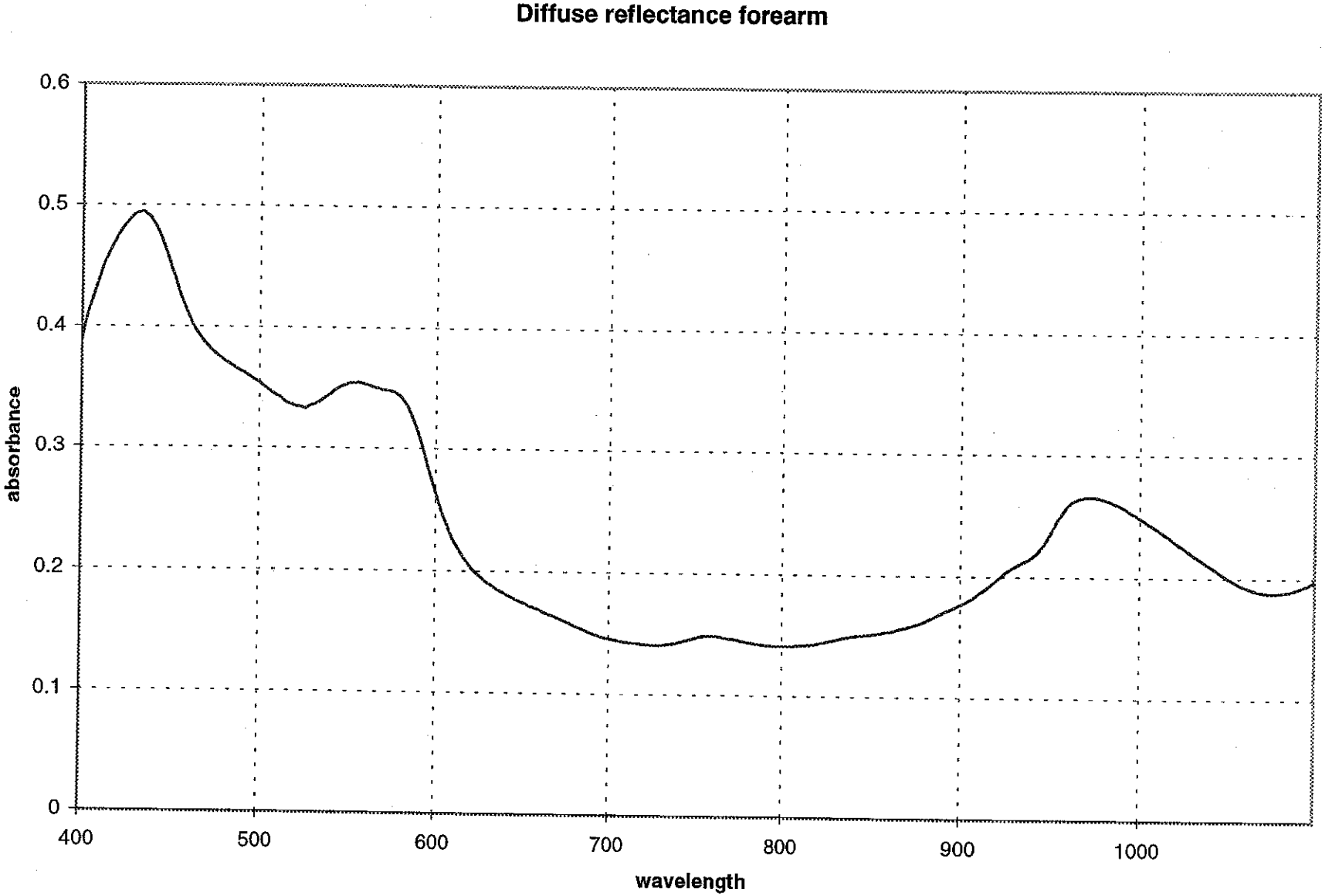
Visible skin transmission




Diffuse reflectance forearm
0.6
0.5
0.4
0.3
0.2
0.1
0
absorbance
400
500
600
700
800
900
1000
wavelength

SALES MEMORANDUM

WHITLAND RESEARCH LIMITED

REGISTERED NUMBER 1475555

Incorporated in England and Wales

SUBJECT TO CONTRACT

INDEX

SECTION 1: COMPANY PROFILE AND INTRODUCTION

Whitland Research Limited is a company specialising in the rapid development of non-invasive medical techniques from invention to the stage of pilot production. It is a company, which matches innovation with commercial need.

Whitland Research (originally called JNA) was started by Professor Dawood Parker in 1989. Drawing on his many years experience in the field of patient monitoring the company has developed extensive links with major research institutes and universities worldwide.

Over twelve years Whitland Research has generated intellectual property (IP) in its own Research and Development Laboratories and acquired other IP from universities and research institutes. In 1999 Steve Turner, a successful UK industrialist, provided Whitland Research with venture capital for the development of technologies, becoming one of two principal shareholders in Whitland Research - the second being Professor Parker.

Renamed Whitland Research Limited in 1999, the company now has a wide non-invasive technology portfolio. A number of leading technologies are at a point in their development cycle where they require a strategy to facilitate full clinical approval and product industrialisation.

The shareholders in Whitland Research acknowledge that the company does not enjoy either the financial resources or business sector experience to fully exploit these technologies in the global market.

Whitland Research Limited is located in West Wales, approximately four hours west of London. Whitland Research currently has five employees, including Professor Parker, as well as university-based consultants.

SECTION 2: TECHNOLOGY OVERVIEW

The strategy of Whitland Research has been to focus on non-invasive patient monitoring techniques. A number of factors have accelerated the demand for non-invasive technologies in preference to the current practice. These are: stress to the sick patient, the risk of infection from withdrawn body fluids, the increasing trend for patients to take legal action against medical staff to satisfy the clinical requirement for point of care diagnosis. All these factors mean that procedures which can remove the need for invasive techniques and provide better diagnostic information are increasingly in demand.

The technologies which Whitland Research has developed have three elements: the sensor, the associated processing and the monitor. Whitland Research has developed technologies in a number of areas. These are listed below, as well as their potential areas of application.

1. **Non-invasive Blood Glucose Measurement**

   Low-cost monitor for use in the home

2. **Non-invasive Oxygen Saturation (SO_2) Measurement with Motion Suppression**

   A number of applications have been identified for this technology:

   (a) Amputation level assessment
   (b) Testing the viability of skin grafts
   (c) Evaluating the rate of wound healing
   (d) Monitoring babies at risk from Sudden Infant Death Syndrome

   This technology has the potential for measuring arterial and venous SO_2, as well as an index of haemoglobin concentration and blood flow.

3. **Non-invasive Oxygen Saturation (SO_2) Measurement and Other Derived Parameters**

   (a) Measurement of SO_2
   (b) Measurement of Carboxyhaemoglobin (COHb)

4. Thermal Imaging for Breast Cancer

A low-cost thermal imager for identifying tumours in the breast and distinguishing them between benign from malignant.

5. Detection of Cardiac Arrhythmias

A low-cost monitor for detecting abnormal heart rhythms and particularly atrial fibrillation.

SECTION 3: PRODUCT DEVELOPMENTS

1. Non-invasive Blood Glucose Measurement

Although several types of blood glucose monitors are commercially available, all are invasive or so-called minimally invasive. For many patients this is inconvenient and discomforting.

There is a need for a non-invasive method of measuring blood glucose concentration to overcome these disadvantages. The ideal glucose monitor should be non-invasive, display a linear response over the range 0 to 30 mmol/L and have a resolution of less than 0.5 mmol/L, have no interference from other metabolites, have a fast response time and should require minimal calibration by the patient. The cost of the monitor should be low.

The absorption of light by biological tissue in the 700nm to 1200nm region is so low that light in this spectral range will penetrate up to 100mm of tissue. It is for this reason that this spectral range is usually referred to as the "diagnostic window" for biological tissue. Light sources and detectors which operate in this region are available at very low cost. Compared with other spectral ranges, this region offers the advantages of high light penetration through tissue and the low-cost of optical light sources and detectors. There is, therefore, the possibility of developing a low-cost, non-invasive blood glucose monitor operating in this spectral range.

We have developed technology for measuring blood glucose non-invasively. A patent has been granted and three patent applications have been filed to date.

We have undertaken extensive in vitro experimentation to determine blood glucose concentration in water, plasma, haemolysed and whole blood. Based on this experience and observations on the optical properties of the skin, we have evolved a technique for measuring blood glucose concentration through intact skin.

We have shown that in the near infrared range (NIR) there is a correlation between the attenuation of light through the skin and blood glucose concentration. Further, we have determined a narrow spectral range of 10nm from which glucose concentration can be determined, a range that makes the measurement insensitive to changes in haemoglobin concentration, blood oxygen saturation and water volume.

We derive a mathematical model from the data in this predetermined spectral range and relate this to the glucose concentration using a predetermined algorithm.

We have compared the non-invasive technique with blood glucose concentrations obtained by analysis of blood samples taken from volunteers. The measurements were made by transmitting light through the finger of the volunteer and measuring the transmitted light intensity. Measurements were made at 5 or 10 minute intervals throughout each test. These measurements were made while, or after, the volunteer had breakfast or lunch (in the case of diabetics), during a Glucose Tolerance Test or whilst eating.

Our results to date indicate that the non-invasive measurement of blood glucose concentration is feasible in diabetic and non-diabetic subjects and is within the Company's target measurement criteria. Evidence suggests that the glucose concentration is derived indirectly from glucose-induced changes in the optical properties of the blood.

With the recent improvement in the patient-to-instrument interface we have shown that in some subjects the patient-specific calibration can remain unchanged for a period of at least a month. Much of the current development is focussed on improving the sensor design.

A prototype is available in our laboratories to demonstrate the performance of the technique.

With the technique we have developed, particularly the narrow spectral range from which our glucose information is derived, it will be possible in the future to develop a non-invasive blood glucose monitor which is based on an LED and detector without the need for a spectrometer.

United States Patent No. 5,553,613, Date of Patent: 10th September, 1996
International Patent Application No. PCT/GB/02127, Filing Date: 2nd July, 1999
United States Patent Application No. 07/743,206, Filing Date: 4th January, 2001
Patent Application filed in the UK in April, 2001
UK Patent Application No. 0013964.2, Filing Date: 9th June, 2000

2. Non-invasive Oxygen Saturation (SO_2) Measurement with Motion Artefact Suppression

Monitors are available which use non-invasive optical techniques to measure the arterial oxygen saturation (S_aO_2) in patients. For example, pulse oximeters are used to measure S_aO_2 by passing light through a finger and monitoring the transmitted signal continuously.

It is well known that these monitors suffer interference due to patient movement, i.e. motion artefact. Movement of the subject leads to a change in the length of the path of the light passing through the tissue and hence to a variation in the intensity of light received by the photodetector. This renders the device incapable of distinguishing between changes in received light intensity caused by variations in light absorption by the component being monitored (e.g. oxygen in the blood), and changes in received light intensity caused by variations in the light path-length due to movement of the subject. The problem is common to all optical monitoring devices and can render these devices inoperative for long periods of time. The problem is particularly severe in critical health care applications, where continuous monitoring is essential.

We have developed an optical monitoring device which measures SO_2 non-invasively and which is insensitive to patient movement.

Further, existing optical devices do not take into account the variations in transmitted light found in varying skin colours. Melanin is present in increasing concentrations from fair to brown or black skin with the result that it can mask the absorption of light by haemoglobin in the dermis. Absorption by melanin is superimposed on that of haemoglobin. The monitoring device that we have developed is capable of compensating for variations in melanin levels in the skin.

The sensor consists of a light source and a photodetector for receiving the light reflected from the tissue. The tip of the sensor incorporates an optical fibre which lies flat on the surface of the skin. White light is transmitted along the optical fibre to the skin where multiple scattering occurs as photons interact with cellular and subcellular particles. Light is absorbed by the haemoglobin present in the blood in the tissue below the sensor before being scattered back along received optical fibres. The scattered light is transmitted along an optical fibre bundle to a miniature spectrometer. SO_2 is computed from a derived algorithm.

The insensitivity to motion arises in the following way: in pulse oximetry a ratio of spectral amplitudes is measured. This approach is very sensitive to movement of the patient. We have developed a multi-wavelength technique which uses pattern recognition to identify the degree of haemoglobin oxygen saturation (SO_2). The use of this multi-wavelength technique makes the measurement insensitive to movement of the patient.

Further, with this technique it is not necessary to contact the skin directly, i.e. remote monitoring of SO_2 is possible. This combination of non-invasive measurement of SO_2 with motion artefact suppression and a capability of measuring remotely makes a number of applications possible:

(a) Amputation level assessment
(b) Testing the viability of skin grafts
(c) Evaluating the rate of wound healing
(d) Monitoring babies at risk from Sudden Infant Death Syndrome

To date we have monitored fourteen newborn babies in Newborn Intensive Care at the Ninewells Hospital, Dundee, for periods of up to eight hours using this technique. The insensitivity to motion was demonstrated when compared with a pulse oximeter.

The technique is currently also in clinical use at Dryburn Hospital, Durham, for amputation level assessment.

International Publication No. WO 00/09004
International Publication Date: 24th February, 2000
International Filing Date: 30th July 1999
International Application No. PCT/GB99/02510

3. Non-invasive Oxygen Saturation ($S0_2$) Measurement and Other Derived Parameters.

As described earlier, we have developed a pattern recognition technique for measuring SO_2 non-invasively. In this method the shape of the measured spectrum is compared using a curve-fitting algorithm to a library of reference curves for different oxygen saturations derived experimentally. In this way the SO_2 can be deduced. As indicated before, this technique allows SO_2 to be measured with motion artefact suppression.

However, we have also observed that the presence of carboxyhaemoglobin in the blood causes a measurable shift in the spectrum. It is possible to determine the percentage carboxyhaemoglobin in the blood from this spectral change. Further, we have observations which indicate that by studying the pulsatility of the spectral pattern it is possible to determine arterial oxygen saturation (S_aO_2) as well as an index of haemoglobin concentration and blood-flow.

Provisional Patent Application No. GB0003152.6. Filing Date 12 February 2000

4. Thermal Imaging for Breast Cancer

Medical imaging is generally understood to mean the imaging of the internal structure of the human body and essentially provides anatomical details of various organs. Functional imaging in contrast involves the imaging of the physiological function of parts of the body. An example of this modality is radioisotope imaging which produces images of the radionuclide - labelled agents of the body. These radiopharmaceuticals are designed to indicate the physiological state of individual organs. The condition of the organ is determined from the distribution of these agents and depends on such factors as blood flow, blood volume and a variety of metabolic processes.

A technique has been developed which applies pixel by pixel analysis to the dynamics of the reheating patterns of skin after a mild cold challenge has been applied. These changes or differences in skin temperature are the result of internal changes. For example, the blood vessels of a patient in a cold room will constrict. If some constrict and others do not, that could be an indication of damage to the nerves controlling that process. Deeper temperature changes will be muted by intervening layers of tissue, so a relatively high degree of sensitivity needs to be maintained.

We have developed a technique which is capable of obtaining thermal images that contain information relating to blood flow. Potential areas of application are in the assessment of blood flow disturbances in patients such as those with diabetes and peripheral vascular disease.

In particular, a potential field of application is that of breast tumour detection where conventional thermography in the past produced an unacceptable number of false positive results. Currently a pilot study is being carried out in order to determine that the new technique can be used to detect breast tumours. Our preliminary results demonstrate that the technique can detect known tumours.

Human skin temperature is lower than core temperature (temperature inside the body) because heat is lost from the body surface to the environment. It is also known that at normal blood flow the temperature on the surface of the breast reflects the heat exchange that occurs at deeper levels in the breast. Therefore, a change in the structure of normal tissue at any depth in the breast, e.g. the presence of a benign or malignant tumour, will result in an altered heat exchange process around the tumour. This in turn will cause a change in blood flow and consequently temperature, at a corresponding location on the surface of the breast.

The method we have developed involves cooling the surface of the breast and then measuring the rate at which the temperature at any particular location on the surface of the breast is restored when the cooling stimulus is removed. These temperature changes are measured using a thermal camera.

The basis of the method is the following:

An exponential equation is derived which fits the variation of the temperature versus time data obtained when the cooling stimulus is removed. The coefficients of this exponential equation are displayed in graphical map form. There are three such coefficients, each representing a specific physiological process. These coefficients provide information about blood flow at the surface of the breast and are used to determine the nature of abnormalities deeper in the breast. In this way, it appears be possible to determine whether a change in blood flow with time at the surface of the breast, is caused by a benign or a malignant tumour.

A demonstration of the technique can be arranged in the laboratory of our research collaborator.

European Patent Application No. 98304752.3

5. Detection of Cardiac Arrhythmias

In a healthy person the heartbeat is tightly regulated by waves of electrical activity that cause the co-ordinated contraction of the heart muscles. Electrical impulses are generated in the Sinu-Atrial (SA) node in the right atrium of the heart. They travel to the Atrioventricular (AV) node, through the Bundle of His and down the left and right Bundle branches, causing the ventricles to beat rhythmically.

In a person with Atrial Fibrillation (AF) the electrical impulses are no longer generated in the SA node but have shifted to some other area of the heart and travel continuously around the left and right atria. This means that they hit the AV node rapidly and unpredictably so that although the ventricles still beat, these beats are 'irregularly irregular'. The result is a 'rippling' effect that makes the heart resemble a bag of wriggling worms.

Atrial Fibrillation is the commonest form of abnormal heart rhythm (arrhythmia) seen in medical practice. Its prevalence increases with age (5% of 65 year olds have AF and almost 9% of the over 80's), as do the associated health problems – it accounts for 33% of strokes in elderly people, causes breathlessness, palpitations and fatigue, and can cause heart failure. Detection of AF in the general population is currently inadequate, late detection adding significantly to health-care costs.

Once diagnosed, treatment of AF is low-cost and highly effective. For example prescribing inexpensive Warfarin tablets can reduce the risk of stroke in AF sufferers by 70%. Diagnosing the condition, however, involves the patient taking an electrocardiogram (ECG) which is expensive in both time and equipment. ECG's are therefore not used for mass screening.

What we have found is that by measuring the pulse interval between successive pulses we can show whether a heart is beating in this 'irregularly irregular' manner.

We have used a prototype monitor to measure time intervals between pulses and have shown in six patients that AF could be identified in this way. Measurements were made through the fingertip and statistically analysed. AF was identified in these patients within 10 seconds.

The monitor we are developing is intended as a first line mass screening for AF. It is intended to be used to indicate if a full ECG is necessary. However, in the future it may be possible to show that it can be used on its own to diagnose AF.

We can produce an inexpensive instrument to identify those patients who need to take an ECG and those who do not. Acting as a pre-screening device, any patient may be tested using this instrument regardless of whether they show symptoms associated with the condition.

- This is an opportunity to develop a product in the short-term at low development cost. We already have some clinical data to show that the technique will work and there is significant market information to show that the product is required.
- A further advantage is that in the short-term we would not claim that the monitor detects AF – we would claim only that it detects an 'irregularly irregular' heart rhythm as a first-line screening method. This indication, however, would call for a full ECG. We are therefore making no claim that we have a diagnostic technique but one that replaces the subjectivity and time involved when a nurse is required to palpate an artery in the doctor's surgery.
- Early detection and treatment of AF can prevent stroke and other conditions costly in terms of health-care. Appropriate treatment of this condition is effective in terms of savings on future care.

The number of unidentified AF patients over 60 in the UK alone is said to be over 300,000.

Patent Application in preparation.

SECTION 4: FINANCIAL SUMMARY

Whitland Research Limited
Balance Sheet
As at March 2001

	£
Fixed Assets	25,053
Current Assets	
Stock	100
Sundry Debtors - Grants Outstanding	26,481
VAT Debtor	1,283
	27,864
Current Liabilities	
Purchase Ledger	10,961
Bank Overdraft	28,967
PAYE Creditor	4,459
Accruals	4,478
	48,865
Net Current Liabilities	(21,001)
Long Term Liabilities	
Directors Loans	123,133
	(119,081)
Share Capital & Reserves	
Share Capital	600
Preference Shares	375,000
Profit and Loss B/Fwd	(287,765)
Profit and Loss Account for Year	(206,916)
	(119,081)

Whitland Research Limited
Application of Funds Statement
From 1st February 1999 to 31st March 2001

	£	£
Grants Received		
Regional Enterprise Grant	24,250	
Spur Grant	12,066	
Spur Plus Grant	180,044	
		216,360
Expenditure		
Research and Developmen	557,011	
Patent Fees	18,881	
Overheads	108,392	
		684,284
Net Operating Loss		(467,924)
Capital Expenditure		
Fixed Assets Purchased		29,956
Funds from Investors		
Share Capital Issued	500	
Directors Loans	123,133	
Preference Shares Issued	375,000	
		498,633
		753
Movement in Debtors/Creditors		
Stocks		50
Debtors		24,040
Creditors		17,639
Cash		(40,976)
		753

APPENDIX 1

PRINCIPAL TECHNICAL STAFF

Name	Qualifications	Job Description
Steve Turner Director		Managing
D. Parker	BSc, PhD, F Inst P, C Phys	R & D Director
A. Holder Engineer	Honorary Research Assistant, National Heart & Lung Institute, Royal Brompton Hospital, London	Senior Project
M. Bowes Engineer	BSc, B.Eng.	Electronic Design
Y. Brown Assistant	BA (Hons)	Clinical Research
J. Bowen Accountant	MAAT, Part Qualified ACCA	Assistant

CONSULTANCY SUPPORT

Dr C.J. Evans, Physics Department, University of Wales Swansea
Consultant in Statistics

Dr D.K. Harrison, Head of Medical Physics Department, Dryburn Hospital, Durham
Consultant in Optical Spectroscopy and Clinical Physiology

CLINICAL COLLABORATORS

Dr T Clutton-Brock, Department of Anaesthetics, Queen Elizabeth Hospital, Birmingham

Dr M. Lewis, General Practitioner, The Kingsway Surgery, 37 The Kingsway, Swansea

Dr J. Pickup, Division of Chemical Pathology, United Medical and Dental Schools, Guy's Hospital, London

Dr D. Price, Consultant Physician, Department of Diabetes and Endocrinology, Morriston Hospital, Swansea

Dr C. Weston, Consultant Physician, Singleton Hospital, Swansea

Dr A. Williams, Renal Dialysis Unit, Morriston Hospital, Swansea

APPENDIX 2

INTELLECTUAL PROPERTY

1. **NON INVASIVE BLOOD ANALYTE SENSOR**
United States Patent No. 5,553,613, Date of Patent: 10th September, 1996

Abstract
This invention relates to a device for the non-invasive measurement of the concentration of a specific analyte in arterial blood. More particularly, the invention is concerned with the measurement of the concentration of glucose in arterial blood.

2. **NON-INVASIVE BLOOD GLUCOSE MONITOR**
International Patent Application No. PCT/GB/02127, Filing Date: 2nd July 1999
United States Patent Application No. 09/743,206, Filing Date: 4th January 2001

Abstract
There is described a device for the non-invasive measurement of one or more analytes in blood in a patient's body part which comprises a light transmitter comprising a plurality of transmitting fibres positioned to transmit light to the body part and a light detector comprising a plurality of light detector fibres position to detect light transmitted through or reflected from the body part. The device especially utilises the non-pulsatile element of a patient's blood. There is also described a method of measuring blood glucose levels and a device programmed so as to calculate one or more of the haemoglobin index, the oxygen index and the blood oxygen saturation.

3. **NON-INVASIVE BLOOD GLUCOSE MONITOR**

Patent application filed in the UK in April, 2001.

4. **ARTERIAL AND VENOUS OXYGEN MEASUREMENT SENSOR**
Provisional Patent Application No. GB0003152.6, Filing Date: 12 February 2000

This invention relates to a method and apparatus for measuring in mammals, both arterial and venous oxygen saturation; and the concentration of carboxyhaemoglobin and haemoglobin in blood as well as blood flow.

5. **GLUCOSE MONITOR WITH SINGLE SPECTROMETER**
UK Patent Application No. 0013964.2, Filing Date: 9 June 2000

6. **OPTICAL DEVICE**
International Publication No. WO 00/09004
International Publication Date: 24th February, 2000
International Filing Date: 30th July 1999
International Application No. PCT/GB99/02510

Abstract
This invention relates to an optical device for monitoring or measuring/displaying the arterial oxygen saturation with motion artefact suppression and to a novel medical technique for providing arterial oxygen saturation data.

7. **THERMAL IMAGING METHOD AND APPARATUS**
European Patent Application No. 98304752.3

The states that were designated in this application are Austria, Germany, Denmark, Spain, France, United Kingdom, Ireland, Italy, Netherlands and Sweden.

Abstract
An apparatus for dynamic imaging of the blood perfusion in skin measures blood flow in human or animal skin non-invasively, by means of processing skin thermographic data. An area of the skin is first cooled, the cooling means is removed, and then, using an infra-red detector, thermographic data corresponding to skin temperature is obtained at a number of points on the area of the skin over a period of time. For each point an exponential fit equation for the variation with time of the thermographic data is calculated. The coefficients of the exponential fit equation are displayed in graphical map form, and the map can be interpreted to provide information about the blood perfusion rate in the skin.

8. ATRIAL FIBRILLATION

This monitor will detect cardiac arrhythmias. Its purpose is to indicate whether an ECG is necessary. In the future it may be possible to show that it can be used on its own to diagnose AF. This is an opportunity for WRL to develop a product in the short-term at low development cost. We already have some clinical data to show that the technique will work and there is significant market information to show that the product is required.

(Patent Application in preparation.)

APPENDIX 3

C V OF RESEARCH & DEVELOPMENT DIRECTOR

NAME: **DAWOOD PARKER**

ACADEMIC POSITION: (to September 1997)
Professor of Physics, University of Wales Swansea
Director of the Biomedical Sensors Unit

CURRENT AREAS OF RESEARCH:

1. Development of a non-invasive, motion, suppressed, oximetry technique for monitoring babies at risk from Sudden Infant Death Syndrome.

2. Development of a Non-Invasive Blood Glucose Monitor.

3. Dynamic Functional Imaging of the Breast as a technique for detecting malignant tumours.

4. Development of Non-Aqueous Colour Indicator Dyes for measuring CO_2 concentrations in medical and industrial applications.

ACADEMIC QUALIFICATIONS:

B.Sc (Hons) Physics and Pure Mathematics
University of Cape Town 1959

B.Sc (Hons) Physics
University of Cape Town 1960

Ph.D.
University of Southampton 1964

Thesis: Photoelectric and Thermionic Emission from Photocathodes

F. Inst. P., C. Phys. 1985

PROFESSIONAL QUALIFICATIONS:

Fellow of the Institute of Physics
Member of Biological Engineering Society
(Past Chairman of Transducers Group)

Past Member of the UK Medical Engineering and Sensors Committee of the Engineering and Physical Sciences Research Council

Past Member of the UK Department of Trade and Industry LINK Molecular Sensors Committee.

ACADEMIC POSITIONS HELD:

1964-1967	Research Fellow, Cancer Research Campaign, University College Hospital, London
1967-1970	Research Fellow, University College Hospital Medical School, London
1970-1975	Lecturer in Medical Physics, University College Hospital Medical School, London
1976-1984	Senior Lecturer in Medical Physics, University College Hospital Medical School, London
1978-1979	Secondment to University of California, Irvine, as Johnson and Johnson Visiting Professor
1982	Appointed Director of Medical Instrumentation Unit, University College, London
1984-1986	Reader in Medical Physics, University of London Director of the Medical Sensors Unit, University College London
1986-1997	Professor of Physics, University of Wales, Swansea. Director of the Biomedical Sensors Unit

INDUSTRIAL POSITIONS HELD:

1978-1979	Visiting Professor based at Critikon Inc., Irvine, CA. (Johnson & Johnson company), involved in the development and production of electrochemical gas sensors.
1981-1984	Founded Physiological Instrumentation Limited, a UK sensor-based company, specialising in patient monitoring techniques. The company was acquired by Novametrix Medical Systems Inc., Wallingford, Conn., in 1984.
1984-1989	Consultant Director of Research and Development, Novametrix Medical Systems Inc., Wallingford, Conn.
1989-1993	Founded Abbey BioSystems Limited, a company involved in the development of a non-invasive technique for the measurement of cerebral oxygenation by optical spectroscopy.

The technology was acquired by Johnson and Johnson in 1993.

1994 Founded JNA Limited, a company involved in the development of the non-invasive measurement of blood oxygenation for monitoring babies at risk from Sudden Infant Death Syndrome and the non-invasive measurement of blood glucose. The latter project was funded by Pfizer Inc., New York.

SPECIAL RESPONSIBILITIES, ACHIEVEMENT OR CONTRIBUTION IN PHYSICS

Special Responsibilities

Head of the Biomedical Sensors Unit, University of Wales, Swansea. This unit was set up on my initiative with the aim of achieving the rapid transfer of medical instrumentation technology to manufacturers of medical equipment.

Achievement or Contribution in Physics

1. Responsible for the development of the first catheter-tip oxygen sensor for continuous oxygen measurement in the newborn baby.

2. Responsible for the development of the transcutaneous sensor for measuring both oxygen and carbon dioxide partial pressures. Sensor is now the standard in transcutaneous O_2/CO_2 monitoring in the newborn.

3. Development of a non-invasive, multi-gas blood gas analyser based on mass-spectrometry.

4. Won Wolfson Foundation Award in 1980 to develop instrumentation for the investigation of cerebral metabolism in the newborn baby by nuclear magnetic resonance and also by infra-red absorption. This project has led to the clinical use of nuclear magnetic resonance to investigate the metabolism in the brain of newborn babies.

5. Won Wolfson Foundation Award in April, 1986 to develop a Pulse Oximeter with motion artefact suppression.

6. Won International Academic Research Support Grant for two years in 1994 from Johnson and Johnson, New Brunswick, USA to investigate "A New Infrared Technique for the Assessment of Wound Healing".

7. Received support from Pfizer Inc., New York for the development of a Non-Invasive Blood Glucose Monitor by optical spectroscopy. Set up research consortium to tackle the problem.

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Since 1993 most of my publications have been in the form of patents. This is because I made a decision to direct my research towards the development of patient monitoring products with research support coming from commercial organisations.

PATENTS

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1996

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FAX FROM

ULTRONICS

ULTRONICS LIMITED
Ultronics House
Athelney Way
Battledown Industrial Estate
Cheltenham
Gloucestershire
GL52 6RT

Direct Line (Tel): 01242 692033
Direct Line (Fax): 01242 692098
e-mail: fiona.henriques@ultronics.co.uk

To: Linda Bertres 001 724 349 8610

From: Fiona Henriques Date: 10th May 2001

No of Pages (inc cover) One

Dear Linda

I can confirm that I have reserved two rooms for 14th and 15th May at the Royal George Hotel, Birdlip, Cheltenham for Pat Cooper and Jeremy Grata.

Telephone number for the hotel is + 44 1452 862506. Fax number is +44 1452 862277.

The rate will either be £85 or £95 per night inclusive of full English breakfast. The rate depends on the availability of either an upgraded room or a standard room.

If I can be of further assistance please let me know.

Kind Regards.

Fiona Henriques

FAX FROM

Whitland Research

WHITLAND RESEARCH LIMITED
Ultronics House
Athelney Way
Battledown Industrial Estate
Cheltenham
Gloucestershire
GL52 6RT

Direct Line (Tel): 01242 692033
Direct Line (Fax): 01242 692098
e-mail: fiona.henriques@ultronics.co.uk

To: Linda Bertres 001 724 349 8610

From: Fiona Henriques Date: 11th May 2001

No of Pages (inc cover) Four

Please find attached copy of the signed NDA.

With regards to the visit of Pat Cooper and Jeremy Grata and their arrival in Cheltenham Monday afternoon. If they get a cab from the station to their hotel in Birdlip – they can check in from 2pm onwards on Monday.

I will leave a message at the hotel for what time I will meet them on Tuesday morning in order to bring them to our offices.

If I can be of any further help please give me a call.

Regards

Fiona Henriques

Jeremy Grata

Full Name:	Steve Turner
Last Name:	Turner
First Name:	Steve
Company:	Whitland Research
Business:	011441242692001
Home:	+44 011441242820467
E-mail:	sbturner@ultronics.co.uk

Jeremy Grata

Full Name:	Dr. Parker
Last Name:	Parker
Company:	Whitland Research
Business:	+44 011441994240686
Home:	+44 011441994240265

MAY 03 2001 AGT:WJ6NQ REC LOC:WBDR1U INVOICE NUMBER:ITIN

BIOCONTROL
625 KOLTER DR
INDIANA PA 15701

J AND L TRAVEL
215 THIRD STREET
CARNEGIE PA 15106

COOPER/PATRICK
GRATA/JEREMY

16 MAY 01 - WEDNESDAY
RADISSON HOTELS 01 NT/S - OUT 17MAY CONFIRMED
RADISSON VANDERBILT 1 ROOM/S GUARANTEE-CREDIT CARD
68/86 CROMWELL RD RATE- 129.00GBP GUARANTEED
LONDON SW7 5BT ENGLAND FAX-44-20-7761-9001
PHONE-44-20-7761-9000 NAME-GRATA JEREMY
CF-0MXFCDB
CANCEL HOTEL BY 4PM TO AVOID BILLING
RATE IS APPROX $185 USD

17 MAY 01 - THURSDAY
US AIRWAYS 741 COACH CLASS 333
DEPART: LONDON/GATWICK 1115A NONSTOP MILES- 3739 CONFIRMED
ARRIVE: PITTSBURGH 245P
SEATS-13C13D LUNCH-SNACK-
TRY FOR BETTER SEATS AT CHECK IN

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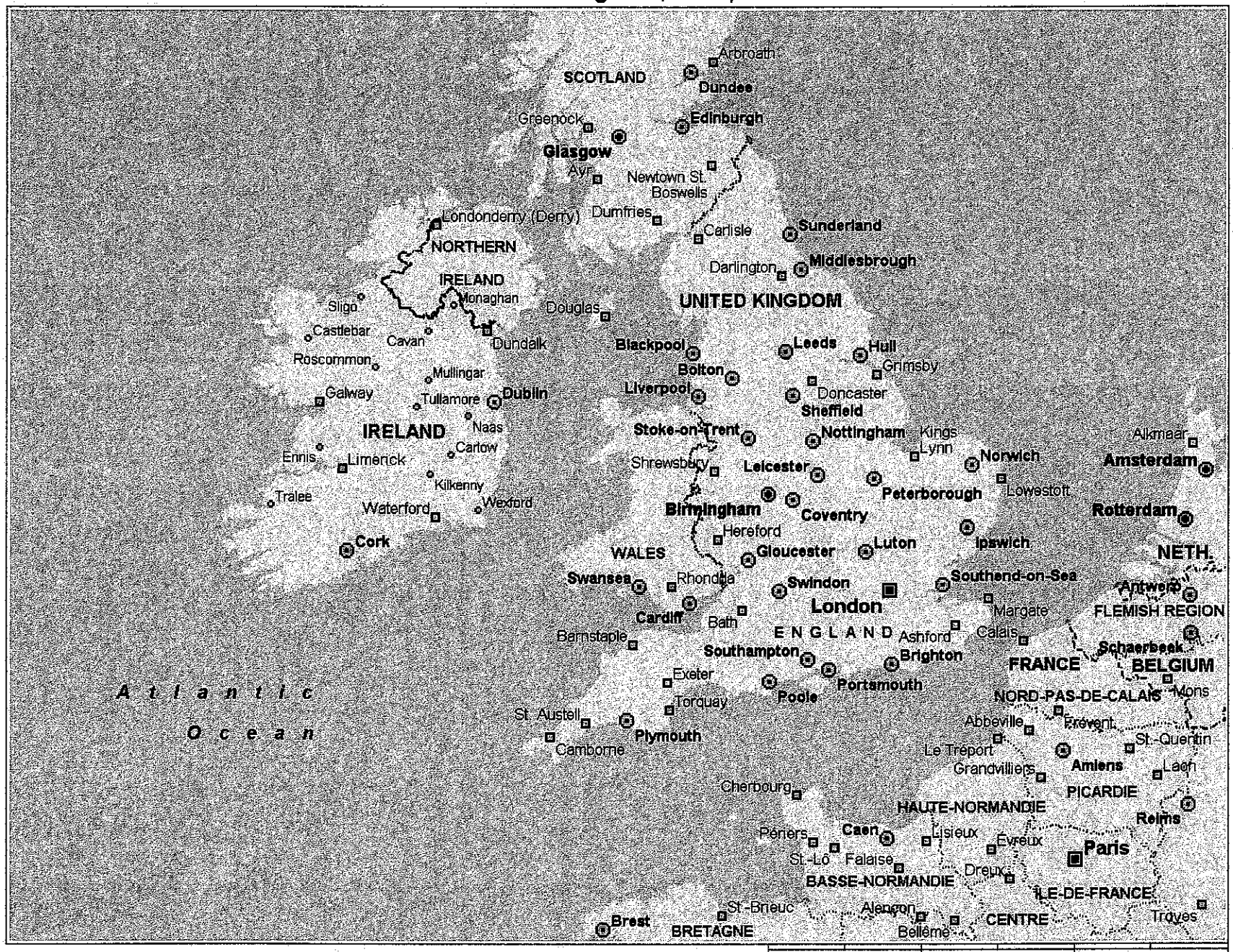
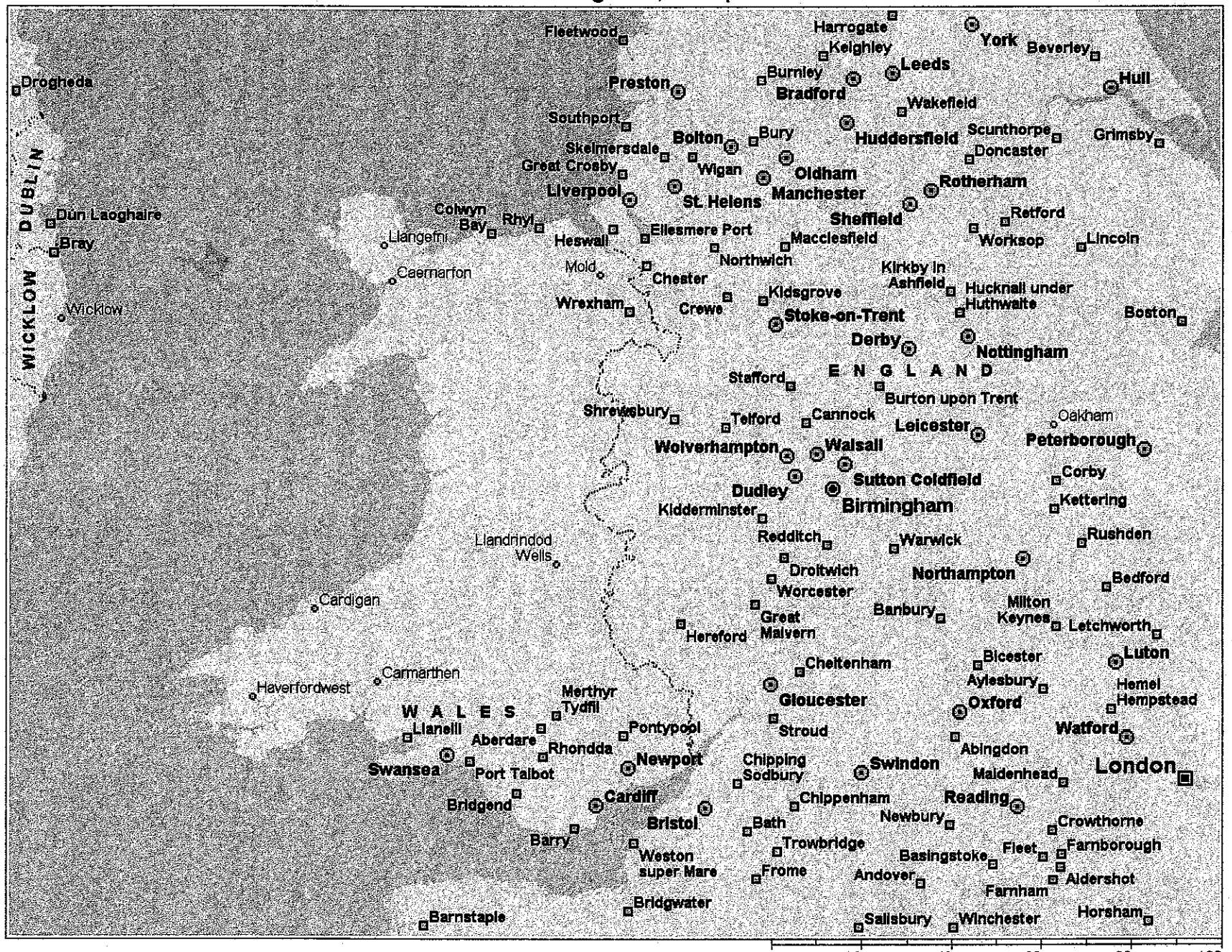
		SUB TOTAL			1517.44
		AMOUNT DUE			1517.44

United Kingdom, Europe



United Kingdom, Europe



MAY 03 2001 AGT:WJ6NQ REC LOC:WBDR1U INVOICE NUMBER:ITIN

BIOCONTROL
625 KOLTER DR
INDIANA PA 15701

J AND L TRAVEL
215 THIRD STREET
CARNEGIE PA 15106

COOPER/PATRICK
GRATA/JEREMY

12 MAY 01 - SATURDAY
US AIRWAYS 740 COACH CLASS 333
DEPART: PITTSBURGH 535P NONSTOP MILES- 3739 CONFIRMED
ARRIVE: LONDON/GATWICK 555A ARRIVAL DATE-13 MAY
SEATS-18D18E DINNER-SNACK-
SEATS ARE IN THE MIDDLE /NOTHING BETTER AVAILABLE
TRY TO CHANGE AT CHECK IN

13 MAY 01 - SUNDAY
RADISSON HOTELS 01 NT/S - OUT 14MAY CONFIRMED
RADISSON VANDERBILT 1 ROOM/S GUARANTEE-CREDIT CARD
68/86 CROMWELL RD RATE- 115.00GBP GUARANTEED
LONDON SW7 5BT ENGLAND FAX-44-20-7761-9001
PHONE-44-20-7761-9000 NAME-COOPER PATRICK
CF-0MXDVPJ
CANCEL HOTEL BY 4PM TO AVOID BILLING
RATE IS APPROX $165 USD

RADISSON HOTELS 01 NT/S - OUT 14MAY CONFIRMED
RADISSON VANDERBILT 1 ROOM/S GUARANTEE-CREDIT CARD
68/86 CROMWELL RD RATE- 115.00GBP GUARANTEED
LONDON SW7 5BT ENGLAND FAX-44-20-7761-9001
PHONE-44-20-7761-9000 NAME-GRATA JEREMY
CF-0MXDVVR
CANCEL HOTEL BY 4PM TO AVOID BILLING
** HOTEL IS LOCATED IN FASHIONABLE KENSINGTON NEARBY ALBERT HALL-
THE VICORIA ALBERT MUSEUM AND HYDE PARK.
HARRODS AND KNIGHTSBRIDGE ARE ON STOP AWAY BY SUBWAY.
ENGLISH COUNTRY HOME ATMOSPHERE/ENTIRE HOTEL EXTENSIVELY-
RENOVATED THROUGHOUT 1999/HOTEL IS RATED 1ST CLASS.
RATE IS APPROX $165 USD

16 MAY 01 - WEDNESDAY
RADISSON HOTELS 01 NT/S - OUT 17MAY CONFIRMED
RADISSON VANDERBILT 1 ROOM/S GUARANTEE-CREDIT CARD
68/86 CROMWELL RD RATE- 129.00GBP GUARANTEED
LONDON SW7 5BT ENGLAND FAX-44-20-7761-9001
PHONE-44-20-7761-9000 NAME-COOPER PATRICK
CF-0MXF8C3
CANCEL HOTEL BY 4PM TO AVOID BILLING
RATE IS APPROX $185 USD

Train:
5/14 From Paddington Station to Wales ~~nonstop~~ direct = no transfers
Destination: Cheltenham, Wales
Depart Paddington 10:36 AM
Arrive Cheltenham 12:43 PM

5/16 Depart Cheltenham 8:08 AM
Arrive Paddington 10:16
OR
Dep Cheltenham 11:22 AM
Ar Paddington 1:25 PM

Mr. Steve Turner will meet you @ train Mon. + make hotel reservations.

MAY 03 2001 AGT:WJ6NQ REC LOC:WBDR1U INVOICE NUMBER: 12968

BIOCONTROL
625 KOLTER DR
INDIANA PA 15701

J AND L TRAVEL
215 THIRD STREET
CARNEGIE PA 15106

COOPER/PATRICK
GRATA/JEREMY

12 MAY 01 - SATURDAY
US AIRWAYS 740 COACH CLASS 333
DEPART: PITTSBURGH 535P NONSTOP MILES- 3739 CONFIRMED
ARRIVE: LONDON/GATWICK 555A ARRIVAL DATE-13 MAY
SEATS-18D18E DINNER-SNACK-
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13 MAY 01 - SUNDAY
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ARRIVE: PITTSBURGH 245P
SEATS-13C13D LUNCH-SNACK-
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ELECTRONIC

AIR TRANSPORTATION	1356.00	TAX	136.44	TTL	1492.44
		SUB TOTAL			1517.44
		AMOUNT DUE			1517.44