Intracranial Hypertension - Condition Monitoring by Time Domain Analysis

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Abstract

This paper discusses the developments in the assessment of intracranial hypertension in humans and recent research carried out by the authors on the techniques for the non-invasive measurement of intracranial pressure. A brief historical review sets the scene with regard to clinical and invasive pressure can be predicted. Although a simulation and a frequency domain analysis of the dynamics of the human brain has been carried out, due to space constraints, this paper concentrates only on the time domain experiments and analysis that were used in developing a non-invasive approach to the measurement of intracranial pressure. The time domain analysis uses the cross-correlation of the non-invasive blood flow of the middle cerebral artery with blood pressure measurements and their varying phase shift with trauma characteristics to make predictions of intracranial pressure trends that lead to pathologically dangerous conditions. The paper concludes with a section concerning the development of software and associated graphical displays that could inform the nursing staff of trends in intracranial pressure and life threatening conditions so that immediate action can be taken.

1 Introduction

Intracranial hypertension is caused by raised intracranial pressure (ICP) which is the pressure that can be measured within the cranial cavity between the outer membrane (dura) and the brain tissue including the ventricles within the brain and the spinal compartments. These ventricles and interconnecting passages contain a lubricating or damping fluid known as the cerebrospinal fluid (CSF). The CSF circulates over the surface of the brain, brain stem and the spinal cord at a rate of about 500 ml/day and has a rate of formation of about 0.4 ml/mm. This means that the CSF is renewed 4-5 times every day. Normal ICP is about 10 mmHg average with dynamic components due to blood pressure and respiration at the same frequencies as heartbeat and respiration respectively. Raised ICP, caused by a pathological condition when the balance of production and absorption of CSF has broken down can go up to 70 mmHg or even higher. Raised ICP can lead to death and therefore monitoring and patient management is very important for any pathological condition leading to intracranial hypertension. Monitoring changes to ICP is particularly important and the anticipation of changes very helpful to clinicians and nursing staff involved in patient management. Intracranial hypertension and craniospinal volume-pressure relationships started back in 1783 by Monro and Kellie in 1824. Munro who was President of the Royal College of surgeons and Professor of Physics, Anatomy and Surgery at the University of Edinburgh made a number of observations in his book entitled “Observations on the Structure and Function of the Nervous System”[l].The original Monro-Kellie doctrine or hypothesis proposed a rigid and extensible cranial cavity, filled to capacity with incompressible brain tissue and blood, from which it was concluded that the volume of the latter must at all times be constant. The doctrine was extremely simple and did not take into account the CSF nor the spinal portion of the craniospinal compartment. Various researchers gradually modified this original Monro-Kellie paradigm

including Burrows in 1846 [2] who postulated that the volume of blood could vary reciprocally with the volume of CSF and Weed and McKibben in 1919[3] who showed that with intravenous injections of hypo and hypertonic solutions the volume of the brain bulk could also be markedly altered. This simple hypothesis did not explain many significant aspects of intracranial dynamics such as the observed effects on ICP by slowly expanding a balloon inside the intracranial vault. Experiments on animals by H Cushing [4] have shown that the ICP rises slowly at first and more rapidly as the volume increases as shown in Fig 1.

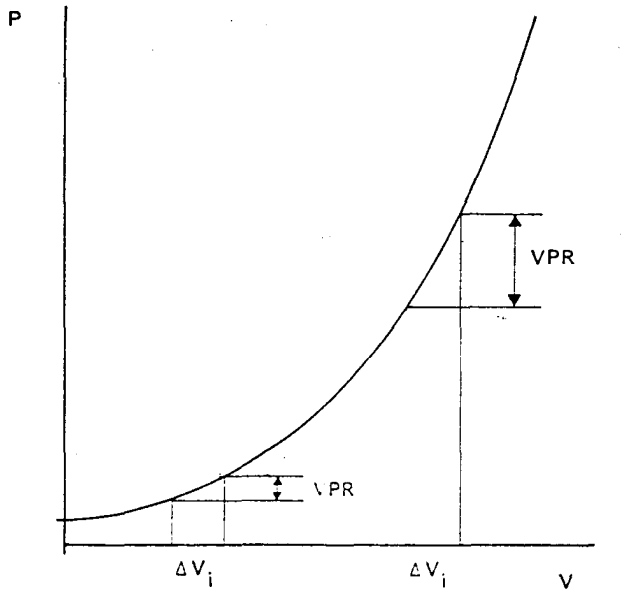

Fig 1

This is explained by the initial changes in volume being accommodated by some change or movement of the intracranial content (probably CSF) and the final effects by exhaustion of the cranial content accommodation and the much increased compressibility of the intracranial contents or the craniospinal covering. Ayala discovered that there existed a relationship between pressure and volume by removing CSF and measuring the ensuing pressure changes. This relationship, known as Ayala's index, is defined as change in pressure divided by change in volume and indicates a type of pathological condition. It has been found to be high with cerebral tumours and low for intracranial hypertension. Weed and Flexner [5] were the first to systematically investigate the changes in total intracranial volume and changes in ICP and concluded that this complex relationship was neither the rigid model nor the pure elastic model. The relationship was perceived to be a function of the collapsibility and distensibility of the dural sac and intra-dural and extra-dural vascular factors. In 1902 Cushing carried out a number of experiments on animals to investigate the effects of local compression as might be caused by tumours and blood clots and general compression caused by hydrocephalus meningitis and subdural haemorrhages [4]. The experiments he conducted used balloons inserted into the intra-cranial space to produce local compression and fluids (salt solution) connected to the cerebral spinal space to produce general compression. Measurements were taken showing that as ICP rises BP rises up to a certain level before death ensues, confirming that a mechanism exists that stimulates the vaso- motor centre to compensate and increase BP and hence blood flow. Ryder et al [6] developed the modem concepts of pressure volume relationships and in 1971 Shulman and Marmaron [7] published a

detailed model which used the collapsibility of the nervous system and not the elasticity of the dural sac as the physiological basis. CSF pulse wave analysis was used by Foltz and Aine in 1980 for the diagnosis of hydrocephalus [8]. They showed that the "pulsatility" of the CSF was augmented in hydrocephalus and argued that this "pulsatility," including the CSF waveform, may be a more valid criterion for the diagnosis of hydrocephalus than mean CSF pressure. To test this possibility, they measured CSF pressures in 118 patients with presumed hydrocephalus and recorded baseline mean pressure and pulse pressure responses to jugular compression, and performed CSF wave analysis (amplitude and peak latency). Four groups of pressure recordings were identified and matched with four clinical groups: normal, arrested hydrocephalus, communicating hydrocephalus, and aqueduct stenosis hydrocephalus. They found that CSF pulse pressure and systolic slope form were highly reliable in the diagnosis of hydrocephalus, whereas mean CSF pressure was not reliable.

2 Measurement of Blood Flow and Velocity

The devices commonly used to measure ICP can be broadly classified into three types: strain gauge diaphragms, pressure sensitive capsules and hollow adaptors with externally-mounted, fluid-tilled pressure transducers and are illustrated schematically in Fig 2. Implanted strain gauge sensors have an electrical connection with the outside world and therefore avoid the problems of blockage that can occur with fluid-filled catheters and adaptors. Traditionally, however, they have suffered from the difficulty or incapability of checking and adjusting the zero level and the calibration when in situ, and have often relied upon inherent stability for their accuracy following their calibration prior to insertion. Catheter tip sensors are sometimes used to measure intra ventricular CSF pressure but more usually they are used in the extramural or subdural spaces. ICP measurement by non-invasive methods using the open fontanelle has been attempted with a number of devices utilising the applanation principle but many of these studies have been compromised by the small numbers of measurements and/or validation of fontanometric pressures against manometric estimation of CSF pressure. The latter technique has a slow response time and a steady state may be difficult to achieve in the populations under study. Applanation fontanometers have also been shown to record increases in measured pressure when subjected to external forces casting further doubt on previous validation studies. Epidural strain gauge transducers were used for all the experiments on humans at Southampton General Hospital.

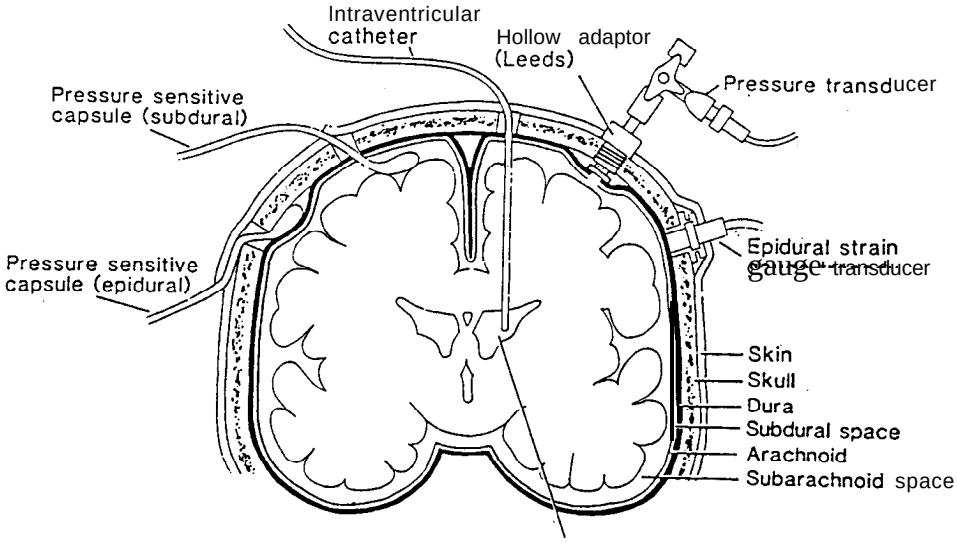

Fig 2.

Doppler ultrasound recording of the blood flow velocity in the extra cranial arteries supplying the brain was reported by Miyazaki and Kato in 1965 [9] and is now used routinely in neurological and neurosurgical practice. The velocity in the intracranial vessels has been observed by Doppler technique during surgery and in children with open fontanelles. In adults, however, the skull is a severe obstacle to the penetration of ultrasound. Bone strongly attenuates the ultrasonic wave, making it impossible to record non-invasively the blood flow velocity from intracranial arteries by conventional Doppler instruments operating in the range from 5 to 10 MHz. At lower frequencies, 1 to 2 MHZ, the attenuation in bone and soft tissues is considerably less. The skull bones are of varying thickness, and because the bone of the temporal region is thin, this would appear to be the most promising area for penetration of ultrasound. Transcranial Doppler sonagraph was used for the measurement of middle cerebral artery (MCA) velocity in all the experiments on human patients at Southampton General Hospital.

3 Time Domain Analysis of Intracranial Pressure

In an intensive care unit, clinical observations of a patient are supplemented by measurements of suitable physiological variables which in general exhibit change or trend before clinical signs of change present themselves. The effectiveness of this measured information is largely dependent upon the method used to communicate it to the nursing staff. A prime objective in presentation of the data should be to enhance the nurses' task and not to burden them with inappropriate information. Periodic measurement and charting of some variables by the nurse ensures that her attention is drawn to the data at regular intervals, with the additional benefits that she may allow her overall clinical assessment of the patient to be included in the charted information and may smooth randomness in the data in a time weighted manner. Only relatively slow physiological changes can be detected by this method, however, and many variables must be measured continuously. Problems then created are how to handle the data, and how to present them to the nursing staff to yield improvements in patient care. Simple display of the measurements have provided valuable information and often enables poor electrode contact or a catheter blockage to be detected from the quality of the signal at an early stage. Since critical illness is characterised by rapidity of change in the time domain it is desirable to provide assistance for the nurse in order to relieve her of the necessity of diligent observation of the primary data. This would be particularly valuable at night when complications occur unexpectedly and when medical and nursing cover is reduced. Some time domain patient monitor systems incorporate an alarm signal which is triggered when the measured variable strays outside limits that are set by the physician to indicate a change in the patient's condition. These have been criticised on the grounds of the high incidence of false alarms that destroy the confidence of the nursing staff This problem frequently results in alarm levels being set so far apart as to be virtually useless. Detection of trends provides the ability to anticipate problems and the modern powerful computers with their Windows driven graphical displays with inbuilt alarms allows such a patient monitoring and nursing indicator to be developed. A simulation of the intracranial dynamics indicated a phase shift between arterial pressure P_a and capillary to venous resistive flow Ir_{cv} which varies with changes to resistance to blood flow caused by accident trauma or invasive tumour growth. By sampling both the arterial pressure and the MCA flow using a transcranial Doppler transducer and storing the data in computer memory, cross correlation analysis should enable the phase difference trend to be calculated and displayed on a continuous basis. There are a few practical problems concerning filtering the incoming data, sampling frequency, sample window and data averaging that will be addressed later in this section but for now we will concentrate on the implementation of a digital cross correlation function to a window of data.

(i) Continuous cross-correlation:-
Fig 3 shows two similar continuous signals phase shifted in time with respect to each other. The definition of the cross correlation of the signal pair is given below :-

$$r_{xy}(\tau) = \int_{-\infty}^{+\infty} f_x(t).f_y(t+\tau)dt$$

(ii) Discrete cross-correlation:-
Based on a time delay of t set, s samples and a sample time of T set the discrete form of the cross correlation function given above is given by:-

$$r^*_{xy}(\tau) = \frac{T}{(s+1)}\sum_{n=0}^{n=s} f_x(nT).f_y(nT+\tau)$$

Based on the above discrete equation, for s samples with a sample time of 20 ms, a table can be constructed in the form of a spreadsheet to facilitate "real time" solution by a digital computer. If we develop a table consisting of a moving window of elements of data taken from a patient in the form of BP (mm H,O) and MCA (mm/set) , a matrix of N x N elements can be produced. The sums of each of the columns represent the cross correlation coefficient at each shifted value in time (the multiplying factor of T/(s+l) does not need to be taken into account as we are dealing with relative and not absolute values). Plotting a graph of the sum of each of the columns against shifted time t yields pictorially the value of t where maximum correlation occurs. A time domain plot of the original raw data is shown in Fig 3 and the graph of the cross correlation function against time shift is shown in Fig 4.

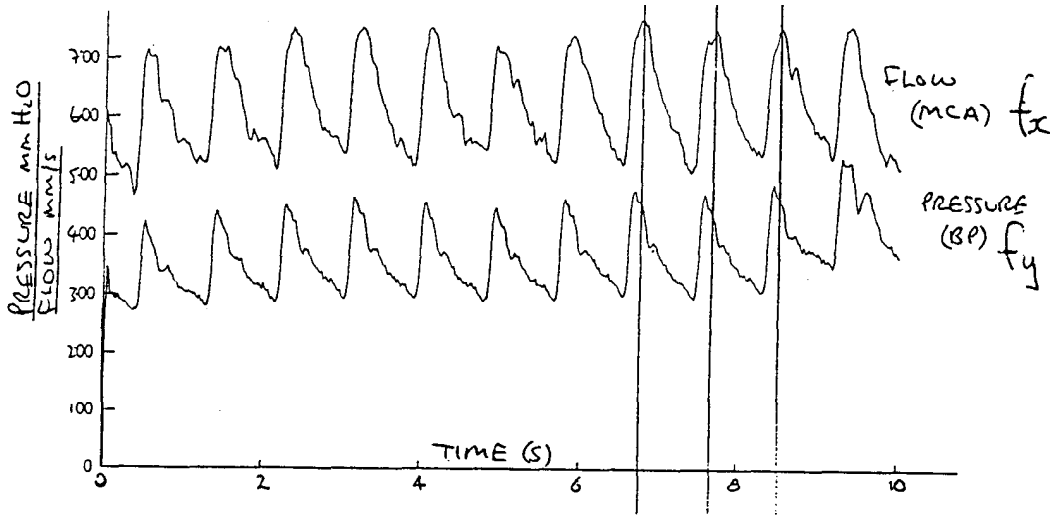

Fig 3.

Although the cross correlation function acts as an averaging or smoothing function all raw data should be filtered as a matter of course to remove unwanted data such as high frequency noise. Since the raw data is imported either from a disc or directly from the data capture unit (A to D convertor and analogue multiplexor) into the computer memory all the signal conditioning can be performed digitally by means of digital filters. A typical signal of BP and MCA flow is shown in Fig 3 above. There are three dominant features associated with this typical signal; a fundamental frequency of about 1Hz; a zero offset; noise. The fundamental frequency is due to the heartbeat and its relative magnitude and phase relationships with other signals is of prime importance. A filter should therefore enhance this feature and minimise all other data. The zero offset although important in itself as an average measure of BP it is not necessary for the time and frequency domain analysis, as we are concerned with relative changes to the beat by beat time variant signal. The noise is also an unwanted signal and needs to be smoothed out as much as possible without too much distortion of the primary signal. To achieve this twofold objective of removing the zero offset and minimising the noise a band pass filter has been employed. This filter has break frequencies at approximately 0.5 Hz (3 rad/s) and 3 Hz (20 rad/s) allowing maximum bandpass over the frequency range of interest. The 's' domain transfer function for this filter is given by:-

$$T(s) = \frac{1/3s}{(1/3s + 1)(1/20s + 1)}$$

The 'z' domain transform for this filter is found from the 's' to 'z' domain relationships and is given by:-

$$T(z) = \frac{e^{-aT} - e^{-bT}}{(z - e^{-aT})(z - e^{-bT})} \cdot \frac{20}{17}$$

where a = 3, b = 20 by comparison with the standard form The sample time T used to collect the patient data was 20 ms. Entering these values into the above equation and multiplying by the sample hold transfer function yields a transfer function given by:-

$$\frac{c}{r}(z) = \frac{(0.32z - 0.32)}{(z^3 - 1.612z^2 + 0.631z)}$$

Cross multiplying, dividing by the highest power of z and replacing $c(z)z^2$ by c(n-2) etc. yields the difference equation given below, from which the digital filter can be programmed in an appropriate language.

$$c(n) = 0.32r(n-2) - 0.32r(n-3) + 1.612c(n-1) - 0.631c(n-2)$$

where c(n) is the current output, r is the input and (n-l), (n-2) and (n-3) refer to values of the variables at -20, -40 and -60 ms respectively. The filtered waveforms using the above difference equation programmed into the spreadsheet containing the original BP and MCA flow data displayed in Fig 3 is depicted in Fig 4 along with the cross correlation function and associated phase shift.

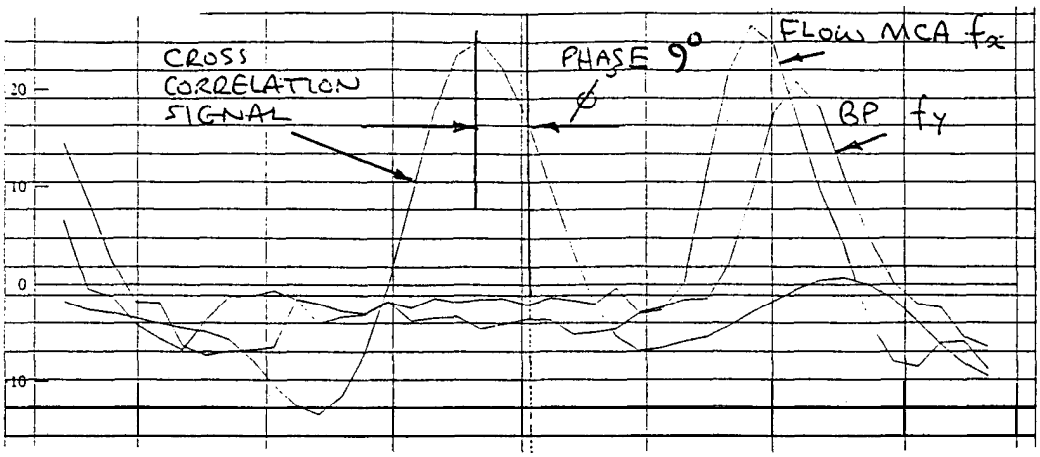

Fig 4.

4 Analysis of the Results.

The simulation of the intracranial fluid dynamics indicated that there should be a trend in phase difference between arterial blood pressure P_a and MCA flow (or velocity as measured by the transcranial Doppler transducer) as the intracranial resistances and compliances change with the progression of trauma. Both of these measurements are readily available from the patient by non invasive methods, as described earlier in section 2 on measurement, which if proved successful will be a safe and useful enhancement to patient bedside monitoring in the intensive care units. Recordings were made of both BP and MCA velocity at Southampton General Hospital and the data stored onto floppy 3.5" disc for analysis at a later date. Spreadsheet analysis was used to both display the data, filter the data using the programmable band pass digital filter and also to perform the cross correlation analysis and display the results. Fig 3 shows the typical raw data for both BP and MCA flow plotted against time. Calibration of the signals is possible the using conversion factors of (0.24.BP - 8.4) mmHg, and (MCA-305)/5.18 cm/s respectively. Fig 4 displays the BP and MCA signals after bandpass filtering and the cross correlation of the two filtered signals. The cross correlation was performed on a matrix of data 90 X 90 (using 20 ms sample times) with an equal overlap of the data either side of the mid point of the sample matrix, allowing the phase shift or time delay between the two signals to be measured with respect to the centre of the horizontal axis of the cross correlation function. Finally the software was embedded into the data collection and analysis system at Southampton General Hospital to enable a continuous indication in the time domain to be displayed along with other vital data such as BP, MCA velocity, heart rate and ICP as shown in Fig 5. This final graph indicates that when a trauma occurs, as indicated by a sudden change in BP and MCA velocity, the calculated phase shift or "pulse transits" predicts that a change in ICP is about to occur. Further work is currently being carried out at Southampton General Hospital on real patient data to verify the initial findings and to develop a new time-frequency display for an improved visual representation of patient health in terms of the calculated time domain phase shift and frequency domain power spectrum.

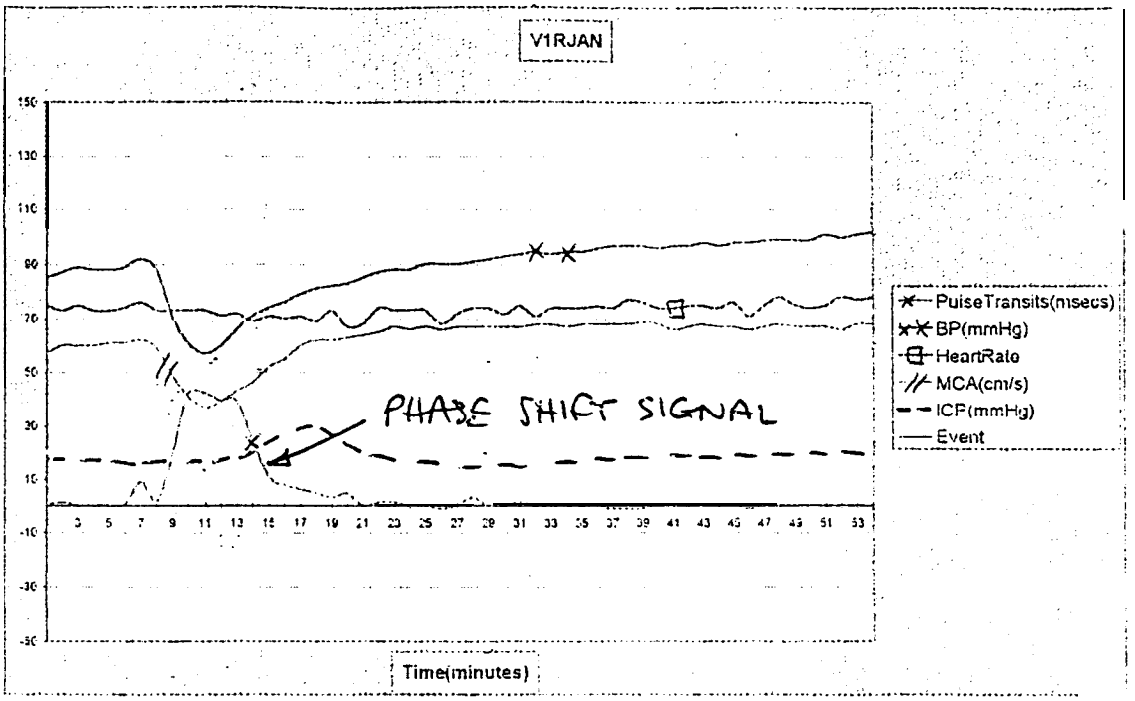

Fig 5

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Richard Penson

Richard Penson graduated from Loughborough University in 1967, with an Honours Degree in Mechanical Engineering. He read for an M Phil at Southampton University (in Control Systems) in 1970 whilst employed by Plessey Aerospace in Hampshire UK. From 1976 he was employed in various industries concerned with aerospace controls and environmental control in both England and Scotland In 1976 he entered education first at Napier University in Scotland and in 1984 at Southampton Institute where he has held the posts of Principal Lecturer, Deputy Head of Engineering, Assistant Director of the Technology School and Currently is Head of Manufacturing Engineering in the Systems Engineering Faculty. His research interests include control systems, signal processing and their applications to medical condition monitoring.

Robert Allen

Robert Allen began his career in the machine tool industry in the 1960's from where he moved to Leeds University to read Control Engineering and upon graduation in 1972 continued at the University to undertake research for a PhD which was awarded in 1978 in the field of modelling the dynamic properties of physiological transducers. Following postdoctoral Research Fellowships in the Departments of Anaesthesia at the University of Leeds and The Welsh National School of Medicine, Cardiff, he moved to the University of Southampton to a newly created lectureship in Biocomputation, a Faculty position in the Faculty of Medicine and horn there to the Engineering Faculty as a Lecturer in Control Engineering in 1984. He has been a Senior Lecturer since 1989.

Robert is a Fellow of the Institution of Electrical Engineers, the Institution of Mechanical Engineers and the Institute of Physics & Engineering in Medicine. His current research interests lie primarily in the medical Engineering and underwater vehicle fields.