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The University of Arizona, 1987
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A CONTROL SYSTEM FOR THE APPLICATION
OF SCANNED, FOCUSED ULTRASOUND IN
HYPERTHERMIA CANCER THERAPY

by
Charles Alan Johnson

A Thesis Submitted to the Faculty of the
DEPARTMENT OF ELECTRICAL AND COMPUTER ENGINEERING
In Partial Fulfillment of the Requirements
For the Degree of
MASTER OF SCIENCE
WITH A MAJOR IN ELECTRICAL ENGINEERING
In The Graduate College
THE UNIVERSITY OF ARIZONA

1987
STATEMENT BY THE AUTHOR

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ABSTRACT

An automatic control system is necessary for use with a scanned focussed ultrasound system to allow a high level of control in the clinical maintenance of therapeutic temperature profiles during hyperthermia cancer treatment. Interfaces and software were created for use with an ultrasonic imager, an RF amplifier, a data acquisition system and a microcomputer to perform the control functions. The software was written in the interest of providing a control scheme for use in both investigative and clinically operative environments. A purely integral type controller was tested at various perfusion and gain values in both in-vitro and in-vivo experiments. Experimental results provide an understanding of the effects of integral gain and perfusion on the quality of control attained with the use of the system. Results also demonstrate the control system's applicability in the investigation of new control schemes and strategies in the application of scanned focussed ultrasound energy.
CHAPTER 1
INTRODUCTION

The existence of the disease we call cancer has been noted since ancient times, and modern man has made extensive efforts in research attempting to find a so called 'cure' for that disease. But, that cure, a technique, chemical treatment or application of energy which will all but guarantee the complete eradication of the disease in any one patient has not been found. To this day many advances have been made toward that end, including the identification of many diseases as types of cancers, new surgical techniques for alleviation of the discomforts of and eradication of cancerous tissues, chemical and radiological treatments aimed towards the same end as the surgical procedures, and progress in identification of the biological characteristics of cancerous cells and tissues.

Scientific research has shown that one therapeutic technique, called hyperthermia, offers a limited hope towards the treatment of cancer in that cancerous cells (single cells and massed cell tumors) have been shown to be susceptible to applied temperature elevations. Reports as early as 1866 suggest a correlation between elevated body temperatures (fevers) and reduction of cancerous cell masses [1]. This led to the development of pyrogenic toxins which could be used to induce fevers in patients and clinical test results showed a measurable increase in patient survival rates due to this
treatment modality. But, the use of ionizing radiation, discovered in 1895, as a treatment modality reduced interest in hyperthermia cancer therapy.

Cell culture methods developed in the 1950s allowed researchers to test the effect of various cancer therapies in a controlled environment. Results of such tests indicate that when cancerous cells are heated to above forty-two degrees centigrade a significant level of cell killing occurs, and a further increase of temperature reduces the time of thermal exposure required to maintain a constant value of cell killing by about one-half for each degree centigrade of temperature elevation [2]. It has also been noted that a combination of treatments, such as radiation therapy used in conjunction with hyperthermia, produces an effect greater than the cell killing obtained with each modality applied separately [3].

A number of methods have been used to attempt heating of cancerous tissues. Whole-body hyperthermia attempts to elevate the patient's entire body temperature to therapeutic levels. This is done by placing the patient within an environment which will induce elevated body temperature for the duration of the treatment. It is considered that whole body hyperthermia will treat not only tumors but metastasized cancer cells as well.

Another method known as regional hyperthermia, is an attempt to heat only the part of the patient which it is assumed contains the cancerous tissues. Only the targeted regions are exposed to the heating modality. This heating method most commonly incorporates
electromagnetic or RF applicators surrounding, as much as possible, the region to be heated, but may also include ultrasound applicators, capacitive applicators, contact RF electrodes, or inductive coils.

A third method uses various interstitial applicators, where the heating antennae or transducer is inserted within the tumor to more locally heat the tissue. These applicators may be radio-frequency needle electrodes, interstitial microwave antennae or ferromagnetic seeds warmed through electromagnetic induction.

Another method, the focus of much research and the topic of this paper, uses the focussed energy techniques. These methods can be described as an attempt to locally heat tissue by focussing energy on a small target volume. By selectively placing the energy in regions of tissue, the methods of focussed energy deposition raise the possibility of controlling the temperature field over the time course of the treatment. Unlike the other modalities which would rely upon the physical properties and configurations of tissue and applicators to provide (or not provide) the desired temperature profiles, the focussed techniques leave open the option of altering the focal location to achieve desired temperature profiles. The greatest advantage of focussed energy methods is the possibility of selectively heating the cancerous tissue and having the healthy tissues remain unaffected. Due to the fact that it has not been shown that all cancerous tissues are more susceptible to heat therapy than normal tissues, the ability to selectively heat tissue volumes and control the temperature field is an important consideration [19].
Early attempts at single point control consisted of input-output schemes designed to control the measured temperature at one point (i.e., maximum measured temperature) by the adjustment of input power after the observation of temperatures obtained in the tissues. This guaranteed control of only one temperature point, and the rest of the temperature field followed a temperature profile governed by tissue properties and power distribution. This use of a focussed power technique helped further advance the theoretical control of tissue temperatures by locally determining the point of highest temperature and controlling its magnitude [14]. This was done considering the use of a microwave system using a set of adjustable amplitude and phase applicators, and optimal feedback control theory on a state-space model based on the "bio-heat transfer equation" [15].

An attempt was also made to focus the effect of a single microwave applicator at a certain depth in a tissue mass by first identifying a one dimensional thermal model for a single applicator broadcasting into tissue over which surface cooling occurs [16], and designing a discrete time controller using two inputs (microwave power and surface temperature) to govern two outputs (temperature at front and back of target tissue) and obtain a maximum temperature within the target mass [17].

A multipoint control algorithm was also developed which assumed an array of energy applicators were to be placed over the tumor location, and the same number of temperature locations were measured within the tissue. The algorithm would use the measured
temperature slope changes at each temperature measurement location during experimental changes in applicator outputs to identify a set of linear equations describing the total system. The identified model would then be used to calculate the optimal power settings for inducing the most uniform temperature profiles with a desired mean [18].

This brief summary of techniques demonstrates a continuing interest in the development of algorithms which can be shown to at least theoretically control tumor temperatures in an optimal manner within the constraints of any one heating modality [14-18]. But, to actually treat cancer patients, it is necessary to develop a clinically useful system which will control the effect of energy deposition and allow the maintenance of tumor temperatures within a range considered therapeutic.

One example of a focused energy method, scanned focused ultrasound, makes use of circular focused ultrasonic transducers allowing the deposition of energy in a relatively small volume of tissue and deep within the patient. Mounting of the ultrasound transducers on a moveable scan arm allows the directing of the energy focus throughout a tissue volume.

A system has been built to allow both experimentation and treatment using the scanned focused ultrasound method for hyperthermia [4,5] (see fig. 1). This system uses an Ausonics B-mode scanner (see sec. 2.1) to perform imaging and patient support functions. The application of the therapeutic energy is effected through a set of large diameter focused ultrasound transducers, the number of and operating frequency of which are selected depending on the
Figure 1  Functional Block Diagram of Scanned Focussed Ultrasound Hyperthermia System
patients treatment location, treatment power requirements, desired penetration depth and the locality of obstructions such as bone and critical tissue regions. The power (ultrasound) transducers are driven with an adjustable four-channel power amplifier [6] which is interfaced with both the HP microcomputer (see sec. 2.4) and the Wavetek signal generator (see sec. 2.5) to allow control of the amplifier. Control of the Octoson® gantry location during treatments and experiments is assigned to an Apple II microcomputer which is interfaced to the gantry's motor driver circuitry through five Anaheim Automation driver units [7]. Image data, in the form of structure outlines, are transferred to the HP microcomputer through a specially constructed trackball/HP interface (see sec. 2.3.1). Temperature measurement in the target tissue mass is monitored through specially constructed thermocouple probes connected to a sensor interface box and read through the HP data acquisition unit [8]. Although the Octoson® gantry location is not controlled during treatments by the HP microcomputer, the gantry's position is monitored through a hardwired connection from the Octoson® motor control circuitry to the data acquisition unit.

Through measurement of tissue temperatures, monitoring of the gantry's scanning location, and adjustment of the amplifier's output power, a constrained control over the temperature distribution in the target tissue mass is effected. Constraints on the effectiveness of the control obtained are the temperature fluctuations during scanning of the power focus [9], target tissue volume [10], chosen scanning pattern [10,13], scanning speed limit [12,13], and transducer
selection [13]. Other affecting parameters are the sampling interval, maximum allowable powers (limited by patient pain), and, importantly, number and location of the thermocouple temperature sensors.

This masters thesis describes the implementation and operation of portions of the scanned focused ultrasound system. An existing Octoson® ultrasonic imaging system and an existing Hewlett Packard data acquisition system, which play important roles in the control scheme, are described for the readers convenience in sections 2.1 and 2.2. Trackball data transfer and amplifier communication circuits, constructed specially for this project, are described along with the software written to allow their use in sections 2.3 and 2.4. A description of the software written in the interest of providing a control implementation for use in the clinic and laboratory is presented in section 2.5.1, and two separate control schemes are described in section 2.5.2. Previously developed in-vitro and in-vivo experimental setups used in the experimental investigations are described for the readers convenience in sections 3.1.1 and 3.2.1. Those experimental regimes were used to test a pure integral controller strategy. Experiments were performed at various perfusion values and at varying gain values and are described in chapter 3. The controller is evaluated in terms of its performance in the experiments and its potential usefulness in hyperthermia treatments. The control system is evaluated in terms of its applicability as an experimental and therapeutic device for the investigation of control of temperature fields in hyperthermia cancer treatment.
CHAPTER 2
SYSTEMS DESCRIPTIONS

2.1 OCTOSON IMAGING SYSTEM

The U.I. Octoson® is a commercially available, automated ultrasonic imaging system. The system, which is a second generation "B" mode echoscope, is capable of producing echograms of soft tissue regions of the body. The Octoson® makes use of multiple (eight), 70 millimeter, 3 megahertz piezoelectric transducers scanning in synchronism, which are mounted on a motor driven, moveable, gantry-supported scan arm inside a large water tank. The water in the tank provides a medium for coupling the imaging transducers' ultrasonic energy to the patient. The patient is positioned over, and supported by, the top of the water tank and coupling occurs through a plastic membrane window. A thin layer of ultrasonic coupling gel, water, or similar medium is used to couple the plastic membrane to the patient's skin. For some applications, the plastic membrane is removed and coupling occurs directly from the water to the patient's skin. Selection of the plane to be scanned and imaged is accomplished by movement of the transducer array which is designed to translate in three orthogonal axes, rotate in the horizontal plane, and tilt in the vertical plane.

The control of the imaging and gantry movement functions occurs from a separate control console. The console contains a black
and white display CRT for image presentation, image quality adjustments, a trackball for user manipulation of screen cursors, and a complete set of gantry positioning controls. The panel control of gantry position and the support of the patient on the tank top provides the capability for accurate and repeatable scanning and imaging. This repeatability and accuracy allows for the production of serial section scans.

2.2 HEWLETT PACKARD MICROCOMPUTER AND DATA ACQUISITION SYSTEM

The microcomputer system used is a Hewlett-Packard 9836A, series 9800, model 236 desktop computer. The desktop unit is equipped with a keyboard and CRT display. The computer's two 5 1/4 inch floppy disk drives are accessed via the system's HPIB internal interface bus (standard IEEE 488, 1978). The computer's backplane has a connector allowing additional external devices to be addressed via the internal bus. The backplane also contains eight edge connector receptacles for the addition of various memory, processor, and interface cards. The main microprocessor is the Motorola MC68000 16 bit data bus processor accessing 200 kilobytes random access memory and a boot read only memory on board.

The computer's backplane edge connector receptacles have been filled with eight user selected circuit cards. An HP 98628A Data-Comm interface card is installed to send/receive data to/from standard RS232C compatible equipment. An HP 98622A GPIO interface card is used to send/receive data in parallel fashion. An HP 98627A color driver interface is used to display color graphics output on a separate Mitsubishi Electric Corporation 19 inch high-resolution color display.
monitor (model C-3920). An Infotek Systems Incorporated FP200 floating point co-processor is installed which allows floating point arithmetic operations to occur 5.8 times faster when programs are written in HP Pascal. Also included in the desktop unit's backplane expansions are two HP 98256A 256 kilobyte and one HP 98257A 1 megabyte memory boards expanding the unit's random access memory to a total of 1.7 megabytes.

Connected to the HPIB is a data acquisition system. The system is composed of an HP 3497A data acquisition unit, an HP 3498A data acquisition unit extender, and an HP 3456A digital volt/ohm meter. The data acquisition unit is equipped with a number of user selected options including six HP 4421A 20-channel relay multiplexers, one HP 44423A 20-channel high speed field-effect transistor acquisition unit, one HP 44425A 16-channel isolated digital interrupt input, and two HP 4429A dual output +/- 10 volt digital to analog converters.

The digital volt/ohm meter is used to measure ac and dc voltages and to make resistance measurements. The voltmeter can be programmed to take and store readings on the occurrence of trigger signals, and with the connection of appropriate data and signaling lines is used to make rapid synchronized measurements through the input options installed in the data acquisition unit.

Also connected to the internal HPIB is a Bering Industries, model 8020, 20 megabyte Winchester type hard disk drive. The hard disk drive is configured such that a 10 megabyte section is used with the HP Pascal operating system and the remaining 10 megabytes is used with the HP BASIC language programming system.
2.3 TRACKBALL DATA TRANSFER

2.3.1 Trackball/HP Interface

As with many commercial imaging devices, the Octoson® allows the operator to manipulate a cursor over the image presentation screen for the purpose of determining the dimensions of structures depicted within the image. This capability is realized using a Measurement Systems, Incorporated, trackball model #622-6-170. This device produces TTL compatible pulses for the Octoson® microprocessor, which translates the pulses into cursor movement on the display screen. In transferring cursor movement to the microcomputer, these pulses are measured and interpreted by the HP microcomputer as representing the outline of significant biological structures within the image. The pulse-data transfer is effected using the HP 98622A GPIO interface card attached to the microcomputer's backplane.

The trackball unit contains two rotary optical encoders and circuitry which presents the encoders output onto four discrete data lines. Each of these lines represents the four directions of trackball movement and relative cursor movement, X+, X-, Y+, Y-. The four data lines are normally at +5 volts with respect to ground. When the trackball is moved, the data line representing that respective direction is driven to 0 volts and back to +5 volts at a frequency of approximately 300 pulses per trackball revolution. The duration of each negative pulse is 40 microseconds +/- 8 microseconds. These pulses are detected by conditioning circuitry in the Octoson® and presented to the Octoson's® processing circuitry.
A block diagram of the circuit, designed specifically for this research, to transfer the trackball data to the HP microcomputer, is shown in Figure 2. The data conditioning circuitry of this trackball to HP interface is hard wired to the four data lines existing in the Octoson's® circuitry. The input stage uses of two SN74LS221 Schmitt-triggered monostable multivibrators. The four data lines are connected to the multivibrators' 'A' inputs so as to detect the negative going transitions occurring on those lines, and are configured so as to produce a negative logic pulse of 420 nanosecond duration. The 'conditioned' data lines at the output of the multivibrators, representing trackball pulses X+, X-, Y+, Y-, are connected directly to the data input lines D10, D11, D12, D13, respectively, of the HP 98622A GPIO interface card in the HP microcomputer's backplane.

The GPIO parallel data interface is designed to accept a hard wired connection from the TTL output pins of the multivibrators and is configured to recognize the +5 to 0 volt negative logic input data by either setting dip switches on the card or through user software. The four 'conditioned' data lines are also presented to a 'clock' generating circuit. This circuitry produces the pulse necessary for clocking the data into the GPIO interface's receive-data register. The circuit performs a negative logic OR with the four conditioned data lines using a DM7408 quadruple 2-input positive logic AND gate package. From the negative logic OR circuitry the signal produced is an indication of the negative transition on any of the four data lines. This signal is then input to two successive multivibrators in one
Figure 2
Functional Block Diagram of Trackball
Data Transfer Circuitry
SN74LS221 package. The first device is configured to produce a 180 nanosecond delay between receipt of the data signal and the triggering of the second multivibrator. The second multivibrator is configured to produce a negative logic pulse of 210 nanosecond duration, whose initial falling edge is the portion of that signal recognized by the GPIO interface as the 'clock' triggering the reading of the four conditioned data lines into its receive-data register.

Also included in this addition is the capability for the operator to signal the microcomputer from the Octoson® console. On the imager's front panel is mounted a three position switch. The switch can be toggled either up or down, or left to rest in its neutral center position. Toggling of the switch causes the triggering of one of two monostable multivibrators whose outputs are tied to DI4 and DI5 of the GPIO interface card. The same lines are also connected to inputs of the OR segment of the clock generating circuitry, allowing the toggling of the switch to be detected by the microcomputer.

Since the image appearing on the screen is related to a real space coordinate system through the position of the imaging transducer array, the position of the transducer holding gantry must also be stored in the microcomputer memory. This is done by measuring voltages in the motor controlling circuits governing each of the five degrees of freedom of the gantry system. The voltage is measured through the high speed FET acquisition channels 60-64 of the HP data acquisition system and the digital voltmeter, and is related mathematically to the actual gantry position.
2.3.2 Data Transfer Software

An HP Pascal language program is used to address the Octoson®/HP interface circuitry and allow the storage of data representing the outlines and positions of significant image features on 5 1/4 inch magnetic disk media. The program, named TRACK, is designed to be used in patient treatment planning procedures to help identify the locations and volumes of various tissue regions for the determination of appropriate scanning patterns during a treatment.

Upon starting the program the user is presented with two pages of information (See Figure 3). The two pages are called as Pascal procedures Msg_1 and Msg_2. Procedure Msg_1 only writes text to the screen. This text informs the user that this program is the one to use when transferring trackball data to the HP microcomputer. It also informs the user that incorrect entries may not be accounted for, that is, it is imperative that the procedures and prompts be followed exactly as directed, and that incorrect entries may cause a loss of data, erroneous data, or a program crash. The procedure Msg_1 also informs the user that the Octoson®/HP communication link, a cable between the 15 pin connector on the back of the Octoson® console cabinet and the HP GPIO interface card in the microcomputer backplane must be connected. It is also noted here that the gantry position measurements are made through the necessary link between the data acquisition system and from the Octoson® motor positioning circuitry. This message appears on the HP microcomputer CRT until the prompted 'enter' key is depressed.
Figure 3  Flowchart: Main Body of Trackball Data Transfer Program
The second procedure, Msg_2, is then called by the HP Pascal main program. This procedure instructs the user as to the proper responses to program prompts, also through text printed to the HP CRT. The text suggests using a fresh, blank 5 1/4 inch floppy disk for each new patient treatment, and explains that the disk should be placed in the right hand disk drive (volume #3 of the HP Pascal operating system). It is also explained that at the appearance of a prompt, requesting the name of a line or a point to be recorded on disk, the user has three options: The response 'HELP' will always return the user to this same page of text, the response 'QUIT' will end program execution, or the entering of a carefully chosen name, of eleven characters or less, will cause the creation of a file on the disk which will contain data representing the named line or point. Here, too, it is explained that after the entering of a file or point name, the 'outline' function switch on the Octoson® console should be switched through the off to the on position. Then the trackball controlled cursor should be moved to the beginning point of the desired line, and the auxiliary switch mounted on the Octoson® console toggled upward one time. Then the cursor should be moved along the desired line. At the end of the desired line, the switch should be toggled downward to save the line on the disk. To enter only a single point, simply do not move the cursor between switch toggling. The procedure Msg_2 maintains the text on the HP microcomputer screen until the prompted 'enter' key is depressed. After Msg_2 is exited a Pascal boolean variable, Quitflag, is set false.
The three optional responses to the line or point name prompt are effected using the Pascal REPEAT/UNTIL construct. This construct is used to repeat a block of commands until Quitflag is detected to be 'true'. The first program statement in the repeated block is a call to the procedure Taknam. The called procedure places the prompt 'WHAT IS THE NAME OF THE LINE OR POINT?' on the computer's CRT and interactively reads the users input into an eleven character string variable Filnam. Then a series of three conditional statements are encountered. The variable Filnam is tested equal to the string 'HELP', and if the conditional is found 'true' then procedure Msg_2 is called and program use instructions are displayed. The string variable Filnam is also tested equal to the string 'QUIT', and if this conditional is found 'true' then the variable Quitflag is toggled to 'true'. The toggling of Quitflag to 'true' is detected by the REPEAT/UNTIL construct's closing statement and program execution is stopped. The third conditional test, which is actually made first within the REPEAT/UNTIL construct, is to test Filnam not equal to 'QUIT' and not equal to 'HELP'. If this condition tests 'true' then a call to a procedure named Transf is made.

The procedure Transf performs the tasks of reading data from the trackball through the HP 98622A GPIO interface card, reading gantry positions at the appropriate times, and storing of the data on the floppy disks. The data collection task is performed in three steps: 1) Institution of an interrupt signaled transfer, 2) Decoding and temporary storage of the received data, and 3) Termination of data transfer and storage of the received data on the floppy disk.
The procedure Transf begins its operation with a call to the system procedure IOINITIALIZE. This procedure causes a power-up reset to occur on all interfaces present in the HP backplane, which means that all software configuration changes made during previous program execution are reversed and the interfaces are set to their power-up or dip switch selected configurations. A data buffer is then created for the storage of data as the data is received through the interface. The data buffer is dimensioned to hold 2165 pieces of data. It had been determined that if it is desired to enter an outline representing the entire outer edge of the Octoson® console screen, 2165 data elements are generated by the trackball while moving the cursor over that outline.

As most data groups will be smaller than 2165 elements, the buffer is large enough for practical operation of the program. After creation of the buffer, it is reset and the end of file marker is set to the beginning of the buffer. The HP procedure TRANSFER_UNTIL is then used to initiate the data receiving operation on the interface. Data is clocked into the interface's receive-data register as it is generated by the trackball data conditioning circuitry. After execution of the TRANSFER_UNTIL procedure, the presence of data in the interface's receive data buffer generates a non-maskable interrupt which stops program execution long enough to compare the received data with an assigned stop-transfer character, record the data into the next available space in the 2165 element buffer, and advance the buffers data-end marker one element (see the flowchart of figure 4). In this application the assigned stop character is the
Figure 4  Flowchart: Transfer-Until Data Receiving Operation
letter 'A', which corresponds to a decimal 65 appearing in the receive-data register. The possible valid data values generated by the conditioning circuitry include the set: 1, 2, 4, 8, 16, 32. Therefore, it is always the case that the transfer will not be stopped by data appearing on the interface.

After buffer and transfer set-up operations, a loop to check buffer content is entered. Included in this loop is a check to see if new data is in the buffer and a conditional which compares a boolean variable Flag to 'true'. If the buffer contains data, the start-of-data and end-of-data markers for the buffer are not found to be at the same element in the buffer. This condition causes the 'buffer-not-empty' conditional to test 'true' and starts the program through steps to decode and manipulate the data. The data is read into a new variable and the start-of-data marker is advanced to the next element in the buffer. The data's decimal equivalent is then determined through a set of comparative conditional statements. The decimal value represents action taken on the Octoson® console as shown in Table 1. The conditional evaluation routine is also shown in Figure 5. When the data is found to be a decimal equivalent of 1, 2, 4, or 8 the X and Y counter variables, which are set to zero at the time the data transfer is initialized, are either incremented or decremented accordingly. This represents trackball movement in one of the four directions of the console screen. If the data is decoded as equivalent to decimal 16, a message is written to the screen that the auxiliary switch mounted on the console has been toggled upward. This also causes the variable
<table>
<thead>
<tr>
<th>DECIMAL EQUIVALENT</th>
<th>FUNCTIONAL MEANING</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>X+</td>
</tr>
<tr>
<td>2</td>
<td>X-</td>
</tr>
<tr>
<td>4</td>
<td>Y+</td>
</tr>
<tr>
<td>8</td>
<td>Y-</td>
</tr>
<tr>
<td>16</td>
<td>SWITCH UP</td>
</tr>
<tr>
<td>32</td>
<td>SWITCH DOWN</td>
</tr>
</tbody>
</table>

Table 1  Decimal Representation of Console Operations
Figure 5  Flowchart: Conditional Evaluation Routine
Linflg to be set true signaling that all following data is to represent an outline on the console which is desired to be stored on the magnetic disk, and the gantry position is recorded by the reading of the potentiometer voltages through channels 60-64 of the data acquisition unit by the digital voltmeter. The potentiometer voltages are converted to $X$, $Y$, $Z$, $R$, and $T$ values and stored as the first five elements in a one dimensional array Dathld. While Linflg is true, all subsequent data representing $X$ or $Y$ direction cursor movement cause not only the adjustment of the $X$ and $Y$ counter variables but also allow the storage of each of the new $X$ and $Y$ values as $X$ $Y$ pairs into the array Dathld. When the data decodes as equal to decimal 32, a message is written on the HP screen indicating that the auxiliary switch was toggled downward, the variable Linflg is set false, and the variable Flag is set 'true'.

The variable Flag being set true allows the buffer examination loop to be exited and the process of saving the data is started. The array Dathld is stored on the magnetic disk as an HP Pascal 3.0 data file whose name is equal to the string variable Filnam which is interactively assigned by the user during execution of the procedure Taknam. The length of the file is determined by the number of data points generated by the movement of the trackball while Linflg is set 'true'. The file is actually a truncated copy of the array Dathld. During the storage of the data on the disk, the message 'WRITING LINE TO DISK' is displayed on the HP microcomputer screen. After the data is stored on the disk the HP Pascal 3.0 procedure IOUNINITIALIZE is
called. This call terminates all transfers currently active and resets all interfaces in the computer's backplane.

2.4 URI THERM-X AMPLIFIER AND COMMUNICATION

2.4.1 Amplifier/HP Interface

The Hewlett-Packard microcomputer is connected to the URI Therm-x amplifier through a serial data interface which allows the control of the amplifiers power output as a microcomputer function. This connection is made by interrupting the RS-232C standard data link provided between the URI-Therm-X amplifier's microprocessor and the Computerwise model TT5 keyboard unit which is used as the amplifier's input/output device.

The amplifiers microprocessor is read-only-memory programmed to receive ASCII coded character data which is presented on the amplifiers receive-data line. Each character so received is examined and the proper amplifier function related to each character is performed. After performing the appropriate function, the microprocessor sends an ASCII coded message out through its send-data line and that message indicates the action taken in the amplifier circuitry.

The TT5 keypad/display unit allows the user to generate ASCII coded characters and subsequently control the amplifiers operation. The character data is sent out via the keypad's send-data line. The display unit also has a receive-data line over which it can collect similar character data for presentation on a two-line, twenty-four column LCD display.
All ASCII alphanumeric and control characters received are either displayed or used to signal a display control function. The keypad/display unit is programmed to send all characters typed in and to display all characters received regardless of their occurrence in time.

The connection to the HP microcomputer occurs through the HP 98628A Data-Comm interface card installed in the microcomputer's back plane. The interface card is configured through toggle switch settings to recognize RS-232C standard data configurations, and outputs its data to such standard specifications. This allows compatibility with both input receivers and output line drivers on the TT5 keypad, the URI Therm-X amplifier unit, and the associated connecting circuitry.

The circuitry designed specifically for this research and connecting the three devices is designed to allow the operation of the amplifier from either the TT5 keypad or the HP microcomputer. This is accomplished by logically 'OR'ing the two send-data lines originating at the HP and TT5, and presenting the result on the amplifier's receive-data line. The amplifiers output is presented to both the HP and TT5 by sending the amplifier's send-data line through drivers to the receive-data lines of the HP and TT5.

The send-data lines from the HP and the TT5 carry positive-logic data with -15 V representing logic 0 and +5 V representing logic 1. These lines are connected to two input pins of an MC1489 MDTL line receiver. The line receiver package
both converts the data to TTL compatible logic levels (range: 0V - 5V), and inverts the logic to a negative state (OV = 1, 5V = 0). To perform a negative-logic 'OR' function, an SN7400 positive-logic NAND package is used. This performs the 'OR' function and reverts the logic polarity to its original state. The data logic is inverted once again through a NAND gate in the same package before presentation to an MC1488 MDTL line driver. The driver reverts the logic once again and presents the data as -12V = logic 0 and +12V = logic 1. The data line is at this point hard wired to a 1N4154 high speed switching diode which, when biased in the forward direction, clamps the output to a +5V voltage supply. The resulting output is a positive-logic data of range: -12V to +5V and is compatible with the URI Therm-X amplifiers line receiver. A logical circuit diagram is shown in figure 6 and the circuits truth table appears in table 2. Note that the truth table state #4 will not likely occur as the HP microcomputer and the TT5 keypad are not used to control the amplifier at the same time.

Transfer of data from the amplifier to both display devices is accomplished by the presentation of the amplifier's send-data line to a receiver input in the same MC1489 package. The -15V to +5V logic is inverted in the receiver and made to be TTL compatible. The receivers output is then hard wired to the inputs of two line drivers of the same MC1488 packages used to send conditioned data to the amplifier. The two drivers revert the logic and present the data at -12V = 0 and +12V = 1. As before,
Figure 6 Logical Diagram of HP and TT5 to Amp Data Line Circuitry
<table>
<thead>
<tr>
<th>STATE</th>
<th>H-P</th>
<th>TT5</th>
<th>OUTPUT TO AMP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 2  Truth Table of Circuit of Figure 6
these two lines are hard wired through two separate 1N4154 high speed switching diodes which, when forward biased, clamp the high logic level to +5V. This -12V to +5V positive-logic scheme is then compatible with each of the receivers present in the HP DataComm card and the TT5 keypad; and represents a carbon copy of the URI Therm-X send-data line output. A logical circuit diagram of this circuit appears in figure 7.

2.4.2 Communication Software

HP Pascal language routines and procedures are used to address the HP/amplifier interface circuitry and allow the control of the amplifier from the microcomputer. Three separate procedures are used to perform common tasks necessary in effective computer control of the amplifier. The procedure Pwrplt, when called, examines the forward and reflected powers reported by the URI Therm-X amplifier and presents the reported values on the HP microcomputer screen. A call to procedure Ampchk results in the amplifier's channel's duty cycle and power supply's voltage current states being coded and stored in appropriate program variable data locations. The procedure Amptlk allows control of the amplifier from the H-P microcomputer keyboard. Amptlk allows both successive keystrokes to be interpreted with the appropriate character data sent to the amplifier's microprocessor and the display of the amplifiers returned message on the microcomputer's video display. The use of these procedures allows sufficient control over the amplifier such that simple character-write functions to the interface
Figure 7
Logical Diagram of Amp to HP and TT5 Data Line Circuitry
are used to step the amplifier through its menu to routinely change the amplifier settings.

The procedure Pwrrpt, a flowchart of which appears in figure 8 and which is used to check amplifier power output, begins by writing the message 'PWR REPORT' to the bottom character line of the HP microcomputer screen. This task allows the observer to know that the power reporting function is occurring. A delay lasting approximately one-tenth of a second then occurs to let the amplifier complete the transmission of any character string elicited by a previous amplifier operation. Then, resetting the HP 98628A interface clears the interface's receive-data random-access memory and places the interface in its power up configuration. A software buffer created by the Pascal program prior to entering Pwrrpt is also reset. This buffer is fifty-three elements in size which ensures ample space for the storage of the entire reported power character string sent from the amplifier. Resetting this buffer simply places the start and end of data markers at the first element and sets the buffer-data flag to its empty state. An HP Pascal language transfer procedure is used to allow the buffer to fill with the new character data. After setting up the transfer, the interface will wait for character data to be sent by the amplifier. When character data is received, an interrupt is generated by the interface and the character is placed into the software buffer. Then, the interrupt is negated and the interface again waits for the next character from the amplifier. This transfer is set up in such a way that it will continue until either fifty-three characters have been placed
Figure 8  Flowchart: Procedure Pwrpt
in the buffer or the transfer is cancelled through another procedure call. After setting up the data transfer, the ASCII coded escape character (decimal 27) is sent to the amplifier via the H-P 98628A interface. It is assumed that the amplifier is not already in its power reporting mode. Upon receiving and processing the escape character, the amplifier returns a character string to the interface which contains control characters for use by the TT5 keypad and the necessary power value characters. An approximate one-tenth of a second delay is used to allow the character string to be received by the interface and placed into the software buffer. Once the message string is in the buffer, it is read and displayed in the H-P microcomputer screen. The video display cursor is positioned to a variable selectable screen location to start the display at the desired place.

The first three characters read from the buffer are control characters to be interpreted by the TT5 keypad and the Pwrprt software ignores them. The fourth through the twenty-sixth characters represent the forward power values for each of the URI Therm-X amplifier channels. These characters include the spaces between the individual channels' powers. Each power value is represented in watts by five characters including a decimal point and, when printed directly to the video display, may appear as the top line in figure 9. The video display cursor is then positioned to another variable selectable location. The next four characters read from the buffer are also control characters to be interpreted by the TT5 keypad and the Pwrprt software ignores them. The thirty-first through the
<table>
<thead>
<tr>
<th>ch. 1</th>
<th>ch. 2</th>
<th>ch. 3</th>
<th>ch. 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forward Power</td>
<td>22.06</td>
<td>22.03</td>
<td>22.11</td>
</tr>
<tr>
<td>Reflected Power</td>
<td>00.10</td>
<td>00.10</td>
<td>00.11</td>
</tr>
</tbody>
</table>

**Figure 9** Display of Forward and Reflected Powers
fifty-third characters represent the reflected power values for each of the URI Therm-X amplifier channels. These characters also include the spaces between the individual channels reflected powers. Each reflected power value is represented by five characters including the decimal point and, when printed directly to the video display, may appear as the bottom line in figure 9.

In other applications, the character data may be used to record the forward and reflected powers for archival purposes in lieu of presenting the information on the video screen. After interpreting and/or storing the power information, another ASCII coded escape character is passed through the interface to the amplifier. This character takes the amplifier out of its power reporting mode and incites the return of another message. Since this message is not used by Pwrrpt, an approximate one-tenth of a second delay is used to let the message fill the buffer and then, as before, both the interface and the buffer are reset. The resetting of the interface also effectively terminates the transfer initiated near the beginning of the procedure Pwrrpt.

The procedure Ampchk begins by creating an input buffer which is nineteen elements in length. During this procedure, which records the amplifier's current operational state, no message is returned from the amplifier that contains more than nineteen characters. Before entering a repetitive loop, a counter variable is set to zero. This loop counter enumerates the runs through the loop which have been completed. Five executions of the code in the loop are necessary to obtain the four individual channel duty cycle
settings and the amplifier unit's power supply setting. Figure 10 shows a flowchart of the procedure and its repetitive loop.

At the beginning of the loop an approximate one-tenth of a second delay is executed to allow any previously initiated response from the amplifier to finish transmission. Resetting the interface clears the present data from the interface's random access memory. Resetting the software buffer then puts the start and end of data markers at the beginning of the buffer. An HP Pascal language transfer procedure is initiated to receive the ASCII coded character data from the amplifier. This is the same type of transfer as that which is used in procedure Pwrrpt and operates on an interrupt basis to fill the buffer with the received character data. After setting up the transfer, an ASCII coded 'enter' (decimal 13) is sent to step the amplifier to either the next channel's duty cycle or the power supply voltage setting. This character's being sent to the amp elicits the return of a message indicating the amplifier's current setting on that channel or the power supply's current voltage setting. The first two characters are then read from the buffer and ignored as they are used as control characters for the TT5 keypad only. The third character is read from the buffer and compared in three ways with the characters 'A' and 'P'.

The first conditional tests for the character being neither an 'A' nor a 'P'. If the character tests 'true' for this condition then the message is proved to be neither one of a channel duty cycle message nor one of a power supply voltage message. Such a case indicates that the amplifier is in its power reporting mode.
PLEASE NOTE:

Duplicate page numbers. Text follows. Filmed as received.

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Figure 10  Flowchart: Procedure Ampchk
and a routine is entered which changes the amplifier's state so that it is either in an individual channel duty cycle reporting sequence or in its power supply voltage reporting sequence. A flow chart of this routine appears in figure 11. To perform this task an approximate one-tenth of a second delay is executed to wait out any existing transmission. Then the interface is reset to clear the RAM and halt any active transfer. The software buffer is also reset to remove any character data from previous transmissions. The previous transfer is again set up so as to allow receipt of the next message and an ASCII coded 'escape' is output via the interface to the amplifier. The 'escape' character drives the amplifier out of its power reporting mode and into its duty cycle and power supply setting mode. An approximate one-tenth of a second delay is executed to allow the new character data to fill the buffer. Then three characters are read from the buffer. The first two characters are control characters used by the TT5 keypad and the third character is the first character of the desired message and is either an 'A' or a 'P'.

The second conditional tests the currently read character as being the character 'A'. When this conditional tests 'true', the message currently held in the buffer is known to be that which is returned when the amplifier is in one of its channel's duty cycle adjustment modes. A routine is then executed which determines the amplifier channel number and the current duty cycle setting. This routine is charted in figure 12. This routine starts by incrementing the counter indicating that one of the five pieces of data necessary
Figure 11  Flowchart: Routine to Take Amp Out of Power Reporting Mode
Figure 12 Flowchart: Routine to Determine Channel Number and Duty Cycle Value
for the completion of procedure Ampchk (see fig. 10) has been obtained. Two more characters are then read and discarded. The fifth character of the message is read and interpreted as representing the channel number whose duty cycle value the message is reporting. This number, 1, 2, 3, or 4, is saved as an index for the array element in which the duty cycle value will be stored. Eight more characters are then read from the buffer and discarded. The fourteenth character is read and its decimal value is stored. The fifteenth character is then read and a conditional test is performed. If the fifteenth character is a blank (decimal 47), the decimal equivalent of the characters ASCII representation is saved as the duty cycle of the predetermined channel. If the fifteenth character is not a 'blank', it is used as the digits portion of the duty cycle representation and the fourteenth character is used as the tens portion of the duty cycle representation. The reconstructed representation is then stored as the duty cycle of the predetermined channel.

The third conditional tests the currently read character as being the character 'P'. When this conditional tests 'true', the message currently held in the buffer is known to be that which is returned when the amplifier is in the power supply voltage adjustment mode. A routine is then executed which determines the power supply voltage by deciphering the message. This routine's flowchart appears in figure 13. This routine starts by incrementing the counter indicating that one of the five pieces of data necessary for the completion of procedure Ampchk has been obtained. Thirteen
Figure 13  Flowchart: Routine for Power Supply Voltage Determination

Start

Diamond: character = "p"

true: 

\[ j = j + 1 \]

Read 14 characters

false: 

Diamond: character = "blank"

true: save \( \phi \)

false: 

Save decimal value of character

Circle

Read 1 character, Voltage := saved value x 10 + current value

Diamond: voltage divisible by 7

false: 

\[ \text{indices := voltage/7 + 1} \]

true: 

\[ \text{indices := voltage/7} \]

Circle

Stop
more characters are then read and discarded. The sixteenth character
is then read and interpreted as the tens portion of the power supply
voltage setting. This character is tested in a conditional statement
comparing it to a 'blank' (decimal 32) to determine if the represented
value is less than ten decimal. The next character is read and
then used with the previous character to obtain the power supply
voltage value. Once the power supply voltage has been obtained,
that value is related to an array index. The approximate average
high frequency output power is tabulated for each combination of
supply voltage and duty cycle in a table contained in the URI
Therm-X amplifier operation manual. This table is repeated in an
array titled Pwr tbl for reference purposes in many of the programs
which require knowledge of the amplifier's power output. The array
index is calculated from the power supply voltage by dividing the
voltage by seven. If the voltage is not evenly divisible by seven,
the index is calculated by dividing the voltage by seven, truncating
the fractional part, and adding a one to the remaining integer.

After five executions of the repetitive loop and all duty
cycle and power supply voltage is obtained, the average single
channel power output is calculated from the array Pwr tbl. The
power supply voltage index and the duty cycle value (used as the
other index) for each channel is used to determine, from the
table, what the approximate power output is for each channel. Then
the four channel's power values are summed and the result is divided
by four. This average channel power value is also saved for reference
purposes.
After execution of the power averaging routine, code is initiated which places the amplifier into its power supply voltage reporting mode. This code is similar to that which takes the amplifier out of its forward and reflected power reporting mode in that a loop is entered in which characters are sent to the amplifier to change the mode, and the returned messages are examined for appropriate characters. The operation of this code is shown in the flowchart of figure 14. This routine starts with an approximate one-tenth of a second delay to allow the completion of any existing transmission. Then, both the interface and the data buffer are reset. A new transfer is started to allow new data to be received in the buffer and an ASCII coded 'enter' (decimal 13) is sent to the amplifier via the interface to elicit the return of a message. An approximate one-tenth of a second delay occurs to allow filling of the buffer. The first characters are read from the buffer and the third character is compared to the characters 'A' and 'P'. If this conditional demonstrates the character is neither an 'A' nor a 'P', a routine is entered to remove the amp from the forward and reflected power reporting mode. This previously described routine is flowcharted in figure 11.

The loop which leaves the amp in the power supply reporting mode is repeated until its last conditional tests 'true', which indicates the third character is a 'P' and the amp is in its power supply reporting mode.

The procedure Amptlk allows the configuration of the amplifier through successive keystrokes performed on the HP microcomputer.
Figure 14  Flowchart: Routine to Leave Amp in Power Supply Volts Mode.
keyboard. This procedure is flowcharted in figure 15. This procedure begins by setting a number of type boolean variables false. Each of these variables will be set true by a separate interrupt servicing routine, procedure Softkeyhook, when the appropriate key is pressed. After the variables have been set 'false', the HP Pascal language procedure IOINITIALIZE is called to put all of the present input/output interfaces in their power-up states. A variable character buffer fifty-four characters in length is then created to accommodate messages returned from the amplifier. After the creation of this buffer, it is reset to place the start and end of data markers at the first element in the buffer.

Once the buffer is readied, a procedure to allow the interpretation of successive keystrokes is instated. This is accomplished by replacing the system keyboard interpreter routine with the procedure named Softkeyhook, the flowchart of which is presented in figure 16. At any time after the installment of the new keyboard interrupt service routine, any keyboard action will cause the immediate stopping of current program execution and the starting of the execution of procedure Softkeyhook. This procedure first checks the boolean flag Doit. If this flag is set 'true', the interrupt is handled by Softkeyhook. The Datain variable is checked to see if the key pressed is one of seven valid keys. If the data is found not to be representative of one of the valid keys, either the original keyboard interpreter program is called to act on keystrokes originally defined or Doit is set 'false', the interrupt is cancelled, and regular program execution is resumed to block any
Figure 15  Flowchart: Procedure Amp1k
Figure 16  Flowchart: Procedure Softkeyhook
function originally defined for that keystroke. When the data is determined to represent any valid keystroke, the Doit flag is set 'false' to signal other routines that the interrupt was handled, and another boolean variable, Keyflg, is set 'true' to allow the procedure Amptlk to detect the keystroke. Through the Pascal CASE construct, the data is conditionally compared to all possible values and an appropriate variable for each represented keystroke is set 'true'. This variable allows the procedure Amptlk to determine exactly which keystroke initiated the interrupt. At the completion of procedure Softkeyhook, the interrupt is disabled and regular program execution is resumed.

The procedure Amptlk uses an interrupt triggered transfer to receive character coded data from the amplifier and this transfer is set up after the keyboard interpreting routine is installed. The transfer operates in the same fashion as the transfers used in procedures Pwrprt and Ampchk, filling the buffer as data appears on the interface. After the transfer is enabled, a single ASCII coded character (decimal 48) is sent to the amplifier to elicit the first message and notify the user of the amplifiers current state.

The program then enters a repetitive loop which is continually executed until the detection of a flag indicating the desire to end the loop (See figure 15). The first task within the loop is to check the buffer for the last message returned from the amplifier. This message is the result of the action taken before entering the loop or the action taken at the end of the last loop repetition. The text in the buffer is read in the same manner as previously described
routines, is displayed on the HP microcomputer screen and notifies the user of the amplifier's current state.

The procedure Amptlk then enters a waiting routine which is executed until the boolean variable Keyflg is set 'true' by procedure Softkeyhook, indicating that a key has been pressed and some other predetermined action must be taken. During this waiting routine, the procedure Pwrrpt is called and executed in loop fashion to provide a constant display of the amplifier's forward and reflected powers on the HP microcomputer screen.

When the variable Keyflg becomes 'true', the waiting routine is exited and Keyflg is set 'false'. An approximate one-tenth of a second delay is executed to allow any current message transmission from the amplifier to complete, and then both the H-P 98628A interface and the software buffer are reset. The resetting of the interface cancels the currently active transfer, and initiates a new transfer which receives messages resulting from the next action.

Along with the variable Keyflg being set true is the setting of another variable. A set of conditional comparisons are executed and that 'true' boolean variable is found. The result of the 'true' testing conditional is the execution of code to take the appropriate action. When the 'true' flag indicates the key pressed is one designed to perform a basic amplifier function, the name of the key is written to the H-P microcomputer screen, the particular flag is set 'false', and the key's character representation is sent in its ASCII coded form to the amplifier interface. Keystrokes handled in such a manner are the enter, space, plus, minus, and
escape keys. The reset key is handled in the same manner except
that no character is sent through the interface as the amplifier
reset function is not implemented as an HP microcomputer keyboard
capability. The quit keystroke is handled by setting the boolean
variable Flag 'true', which signals the need to exit the Keyflg
interpretation loop. The quit keystroke also causes the procedure
Softkeyhook to be disabled and the original keyboard interrupt
service routine to be installed. Note that when a key other than
quit is interpreted, the message elicited from the amplifier is
handled at the beginning of the next execution of the program's
outer loop.

The majority of the procedure Amptlk is confined within an
HP Pascal TRY/RECOVER construct allowing the trapping of errors.
If a system error, either user or equipment generated, is encountered
the RECOVER block, flowcharted in figure 17, is executed. This
block of code ensures reinstatement of the original keyboard
interpreter and the resetting of all interfaces before exiting.

2.5 CONTROL SYSTEM DESCRIPTION

2.5.1 Control Implementation

Implementation of the control schemes, two of which are
described in the next section, is accomplished using a main program
which calls numerous subroutines. Each control scheme is an
adaptation of a specialized subroutine called by a main program.
The main program executes in a linear fashion without loops or
Figure 17  Recover Block of Procedure Ampchk
endpoints and calls each major segment of program operation as a single subroutine.

The first subroutine called in the main program, flowcharted in figure 18, is Msg_2, which essentially introduces the program by writing text to the screen. This text explains the program's purpose and cautions the user to take care in responding to the program prompts, as not all possible incorrect entries are accounted for. Routine Msg_2 ends with a call to procedure Pause, which simply requires the user to type the enter key to resume program execution and move on to the next page of displayed text.

The next subroutine is also designed solely for the purpose of writing text to the screen. This text introduces the procedure Amptlk described in section 2.4.2. This subroutine, Msg_3, instructs the user to reset the URI Therm-X amplifier by depressing its front panel switch. This routine also lists a key function correlation table which explains which HP microcomputer keyboard keys are used to effect the various amplifier commands. Msg_3 also labels an area of the screen for the reporting of the amplifiers power by procedure Pwrrpt which is called by procedure Amptlk.

The third codeblock called from the main program is the procedure Amptlk. The call to Amptlk at this point allows the user to set the power amplifier at the particular configuration desired for the current treatment. The routine operates in the manner described in section 2.4.2 and allows setting of the amplifiers reference signals, duty cycles, and power supply voltage exactly as described in the URI Therm-X operating handbook.
Figure 18  Flowchart: Main Program Used to Implement Control Schemes
The next procedure called is Defset. This procedure is a series of assignment statements used to set the program parameters to their default states. Typical parameters set in this procedure are treatment times, reading intervals, data output files, control algorithm constants, and operational mode flags.

The next call from the main program is made to procedure Setpar. This procedure allows the user to interactively change some of the parameters set in the procedure Defset. Setpar (flowcharted in figure 19) begins with a display of text to the H-P microcomputer screen. This text informs the user of the function of the subroutine, that any response of '999' will restart the subroutine, and that a response of '0' will be interpreted as accepting the displayed default value as previously set. Next, a case counter 'j' is set equal to 1. This variable is used in a series of two Pascal case constructs to request a value from the keyboard and to set the variable in memory. The first case block prompts for the parameters new value and prints the current, or default value to the screen. Between the two case blocks is a keyboard input read operation. The value input is compared to the integer 999. A 'true' testing comparison conditional results in an error flag being set 'true'. This 'true' set flag leads to all other operations being bypassed and a Pascal REPEAT/UNTIL construct surrounding the procedure starts the execution of Defset again. A 'false' testing conditional results in the error flag being set 'false' and execution of the remainder of Defset is enabled. The second conditional simply sorts the parameter and sets the currently active
Figure 19  Flowchart: Procedure Setpar
Figure 19 (continued)
parameter equal to the input. Both case constructs contain n case
tasks where n is the number of integer type parameter variables
needed to be set before the control strategy's execution. After
the second case block, the variable j is incremented and then
conditionally tested in the boolean expression (j=n+1) OR (flag=true).
This is effected with a REPEAT/UNTIL construct and allows the
execution of the pair of case statements until all parameters have
been either set or accepted.

Once the program parameters have been set, the error flag is
checked to enter the output file name acceptance block of code. On
finding the flag set 'false' the user is prompted for an output file
name. Up to twenty characters plus an 'enter' are read from the
keyboard and saved in a character variable. This variable is then
conditionally compared to the character string '999' and a true
result causes the error flag to be set 'true'. A 'false' result
ensures the error flag to be set 'false' and the input file name is
conditionally tested in the boolean expression (filnam not equal to
zero) AND (flag equals 'false'). A 'true' result of this comparison
enables the input character variables being passed to the HP filing
system and the character variables use as a data output file name.

After assignment of an output file name the error flag is
again conditionally compared with the boolean state 'false'. A 'false'
error flag at this point allows execution of code which provides
the user with a means to verify his acceptance of the program
parameters. The parameters and their labels are printed to the
screen and the user is prompted to verify their acceptance. A 'no' answer will set the error flag 'true' and the procedure Setpar is started again. A 'yes' answer allows the error flag to pass through the final procedure conditional as 'false', and the procedure Setpar is exited.

The next procedure, Validtcpl, provides the user with the option of turning specific thermocouples on or off. This procedure requests that the number of any thermocouples, for which it is desired to have their output ignored, be entered into the keyboard. The procedure simply toggles an element of an array Valid from either zero to one or from one to zero. Any data storage or screen writing program will, during the course of execution, check the array Valid to determine the validity of data from each represented thermocouple, and treat the data accordingly.

The last major procedure called before the execution of a control strategy is Scrset. This procedure configures the screen for the presentation of data during treatment and consists only of text writing operations directed to the HP microcomputer screen. Scrset labels areas reserved for display of the treatment time, amplifier powers, temperature readings measured with the thermocouples and various program operating modes and interactive key function correlation tables.

The procedure Pause, described earlier, is then called to hold the program at the point just before execution of the particular control strategy implemented in the procedure Strtcik.
Strtclk, whose block flowchart appears in figure 20, is executed in three major segments, an initialization block, a TRY block, and a RECOVER block.

The initialization block of Strtclk contains code essential to the implementation of a particular control strategy which must be effected before control can occur. In this block a call to the HP Pascal I/O initialization routine is made to put all interfaces into their power-up default states. Here, also, the keyboard and timer interrupt servicing routines (ISR) are redefined. The keyboard ISR is replaced with a routine Keyhook2 which essentially locks out all but a few user defined keys designed to allow interactive alteration of program parameters during the treatment or TRY block. Such parameters include the target temperature and manual-feedback control modes. The timer ISR is defined to set a boolean flag variable to indicate that a timed event (eg: thermocouple reading) is requested during a treatment. Also, in the initialization segment, a number of major event marker variables are set. These markers correspond to the number of timer interrupts which must occur before power-off and end-of-treatment modes are entered. In this block, the control parameters such as the power supply voltage, maximum power step, and reading interval are converted to a form suitable to control algorithm use. Boolean variable flags are set to indicate starting modes, enable the power-on state, enable the first thermocouple reading, and disable changing of the amplifier settings. String variables used in the thermocouple reading routines are first blanked and then set to reflect the desired data acquisition
Figure 20

Block Flowchart: Procedure Startclk
unit channel numbers. The final task in the initialization block is the configuration and implementation of the timer interrupt sequence immediately followed by a clock read for noting the start of treatment time.

The TRY block of code is the working part of an HP Pascal TRY/RECOVER construct. This is the segment which in this implementation contains the code effecting a particular control strategy. These control strategies are to be discussed in detail in the next section. The TRY block is exited in only one of three ways: 1) The complete execution of all code in the TRY block allows the RECOVER segment to be skipped and execution resumes at the first line after the RECOVER block; 2) An HP Pascal system detectable error occurring during the TRY block immediately halts execution and execution resumes at the first line in the RECOVER block; or 3) An HP Pascal procedure call to ESCAPE(0) immediately halts program execution and execution resumes at the first line in the RECOVER block. The control strategies quit the TRY block with a call to ESCAPE(0) at the end of treatment time, but, the keyboard generation of a system detectable error may be effected through the instated keyboard ISR to stop the data gathering and control strategy at any time before the end of the treatment.

The RECOVER block handles error trapping functions and end-of-treatment tasks. The most important task is the power-off function. This HP Pascal GPIO interface control register write procedure causes an output line to change states and disable the power supply output. Other functions of this block are the reinstatement of the
original system keyboard and timer ISRs and the uninitialization of the system I/O capabilities.

The last procedure called from the main program is Datwrit which takes care of writing of the treatment data to a data storage medium. This procedure first writes text to the H-P microcomputer screen asking the user to ensure that the storage device is on line. The procedure Pause is used to hold program execution until this is done. The program continues execution with the opening of a file with the name entered in Setpar and the treatment temperature data is saved along with the characteristic parameters of the treatment.

2.5.2 Control Schemes

Each control scheme is implemented as a block of code placed within the procedure Strtclk described in section 2.5.1. Two different control schemes are described in this section. The first attempts to effect control through the measurement of a tissue temperature field and the adjustment of the URI Therm-X duty cycle settings. This scheme is implemented in program CONTROL_1. The second scheme, implemented in program CONTROL_2, effects control through the measurement of a tissue temperature field and the adjustment of a Wavetek function generator's output duty cycle settings. Both schemes perform a number of similar functions but the organization and decision making constructs differ between the two.
Each control scheme is written in such a manner that the insertion of different control algorithms may be made with relative ease. The first algorithms implemented operate under the assumption that an appropriate scanning pattern has been selected and the ultrasonic energy is focussed so as to elevate the temperature of a tissue volume in which a controlling thermocouple is mounted. Thus, the effect of scanning and applying power is monitored as changes in temperature at that thermocouple.

The measured temperature is used in the controlling algorithm to determine the change in output power and the new applied power value by adjustment of the amplifier's output duty cycle according to the following formulas:

1) \( \text{change in duty cycle} = a \times (\text{target temp} - \text{measured temp} - b \times (\text{measured temp} - \text{last temp})) \),

2) \( \text{new duty cycle} = \text{old duty cycle} + \text{change in duty cycle} \),

3) \( \text{power output} = \text{new duty cycle} \times \text{amplifier maximum power} \).

There is a large element of memory in the algorithm due to the calculation of a 'change' which is added to the current power supply duty cycle. The scalar 'a' is a multiplier gain constant which proportionally affects the magnitude of the calculated change. This gain will determine the aggressiveness of the controller and is determined prior to each treatment. The scalar 'b' is a multiplier gain constant which proportionally affects the influence from the slope of the temperature trajectory on the calculated change. When 'b' is a positive value, an adjustment in the calculated change is
made which actively reduces the slope of the temperature trajectory. When \( b \) is identically zero, the controller becomes one of a purely integral type. When \( b \) is not zero and the temperatures measured at the last and current reading intervals equal the targeted temperature, no change is made in the duty cycle setting.

The control algorithm's calculated new duty cycle is adjusted to within the range 0.0-1.0 by setting any duty cycle calculated as less than 0.0 equal to 0.0 and any duty cycle calculated as greater than 1.0 equal to 1.0. The limits of the power applied are then zero watts at cutoff and a saturation at the power amplifier's maximum power value due to the current power supply voltage setting. Therefore, judicial selection of that maximum power supply voltage setting should be made prior to the start of a treatment.

Due to the necessity of turning off the applied power for a finite interval of time (1 sec.) before the reading of the thermocouple's temperature, the interval of time between the successive thermocouple readings is maintained at or above ten seconds. These long sampling intervals are used to minimize the percentage of the total time during a treatment that the power is turned off. Thus, the time between two consecutive sampling events will typically consist of first one to two seconds of power-off time during which thermocouples are read and then the remainder of this time period is filled with the application of the power at the newly calculated duty cycle.

A fourth variable, (aside from gain, power supply setting, and sampling interval), which affects controller performance is the scan period. The scan period, or interval at which the focus of
power passes the thermocouple, is a direct function of the scan pattern (i.e., scanning path and scanning speed). The scan pattern is dictated by such constraints as treatment site volume, site configuration, and site accessibility. It follows that the scan period, like the other controller affecting parameters, is determined before treatment. These parameters are set to a default value in the procedure Setpar.

The first control scheme is implemented in program CONTROL_1 and is flowcharted in block diagram style in figure 21. This strategy uses the HP Pascal TRY/RECOVER construct to repetitively execute a series of seven boolean comparisons.

The first comparison tests the boolean variable Servflg. This variable will test 'true' after the occurrence of a clock generated interrupt. The HP Pascal system provides for the generation of a clock interrupt through a procedure call made in the initialization block of procedure Strtclk. The call to TIMERIOHOOK is made to set the system's cyclic timer at an interval equal to the reading interval entered during the execution of procedure Setpar, and to replace the system timer ISR with a new ISR titled Service. On the occurrence of any timer interrupts, which then appear at frequencies determined by the user-set reading interval, program execution halts and ISR Service executes to set the boolean variable Servflg 'true' and increment the interrupt counter variable. Program execution then immediately resumes at the point where the interrupt occurred, after which the variable Servflg will test 'true'. This 'true'
Figure 21  Block Flowchart: Control_1 Controller Scheme
testing conditional results in the execution of a block of code performing tasks required at each clock interrupt.

The timer interrupt tasks code is flowcharted in figure 22. First, the HP microcomputers real time clock is read and the treatment time is stored. A character string is then sent through the HPIB to the Wavetek function generator disabling its output and effectively turning power off. The thermocouples are read through the HP data acquisition system and the calculated temperatures are stored in a holding array [8]. After temperature reading the variable Power is tested to determine if the power should be reenabled. A 'true' test results in the Wavetek's output being reenabled through an HPIB character write procedure. At this point, the temperature data is written to the HP microcomputer screen with a call to procedure Scrwrit. The procedure Scrwrit is simply a series of write procedures which direct the placement of temperature values to the labeled, reserved locations on the screen. After writing the temperatures a conditional test is made to determine if the end of the treatment's heating period has occurred. This is done by checking the result of multiplying the interrupt counter by the reading interval and comparing the resultant magnitude with the user selected end of treatment time. If this test yields a 'true' result, the power is turned off, the variable Power is set equal to 'false', and the mode indicators corresponding to the respective treatment times are written to the screen. Similar screen tasks are performed when the conditional tests 'false' and the power is left in its off state.
Figure 22  Flowchart: Timer Interrupt Tasks
The last clock interrupt task is to set Servflag 'false' and to set Changeamp 'true'.

The second conditional comparison in this control scheme tests Changeamp and Power both as being 'true'. This indicates the necessity for execution of a block of code to calculate a new power supply setting and effecting that new setting in the URI amplifier unit (see figure 21). This is the only active portion of the entire program as it is in this block that the control algorithm is placed and the product of the control is effected.

A flowchart of the control calculation appears in figure 23. The control calculation routine first sets the boolean variable Changeamp to 'false'. Then the actual controller calculation described earlier takes place. The result of this calculation is a desired change in the power applied to the tissue. This change in power is adjusted subject to several constraints. A calculated change of zero is adjusted to the value 999. A change value of 999 signals the remainder of the power adjustment algorithms to not execute and helps save the time used there for other program tasks. The boolean variable Bumpless is checked to determine if a switch from manual to feedback control has occurred since the last iteration of the REPEAT/UNTIL construct in the TRY block of procedure Strtclk. The calculated and adjusted change is then written to the HP microcomputer screen. The value of Change is then again adjusted to reflect the limits of the variable Maxstep. This variable is calculated from the value called sensitivity which is interactively set during execution of the procedure Setpar. Maxstep limits the
Figure 23  Flowchart: Control Calculation
Figure 23 (continued)
maximum power supply change during a single reading interval. Then two consecutive comparisons are made to determine the sign of the value of Change. The result of the comparisons are that the change is set equal to the change plus the current power, the power supply value table, Pwrtbl, is searched for the next value greater than Change in the direction corresponding to the sign of the change, and the resultant duty cycle and power supply values being stored in memory. In the case that the variable Bumpless is set equal to 'true', the procedure Ampchk is used to determine the amplifiers setting, the array Pwrtbl is used to calculate an average channel power setting, and that average value's settings are used to approximate the current power supply value for use during the next control calculation sequence. After the final change calculations have been made, a routine to leave the amplifier in its power supply reporting mode is executed and the duty cycle changes and duty cycle values are written to the HP screen.

Once the new duty cycle values have been calculated, they are effected through code which changes the amplifier's settings. A flowchart of this code appears in figure 24. A variable j is first set equal to one. This variable is used to count the number of iterations through a loop which adjusts the amplifier's duty cycle and power supply voltage. Five iterations are required, corresponding to the four duty cycle and one power supply setting. Within the iterative loop, the HP Data-Comm interface is reset. Then the input buffer previously set up for data communications is reset and a delay is initiated to allow any active transmissions to
Figure 24  Flowchart: Power Adjustment Tasks
The amplifier is at this point in its power supply reporting mode and an ASCII 'enter' character is sent to step to the first channel duty cycle setting. The sign of the change in duty cycle is then checked in a series of two conditional comparisons. The result of these comparisons is that a variable $i$ is set equal to one and another repetitive loop is entered. This loop contains a short delay and either an ASCII 'plus' or 'minus' is sent to the amplifier according to the sign of the change. The variable $i$ is then incremented and compared in a calculation to determine if the number of characters sent equals the number of steps required to effect the calculated duty cycle changes. When the channels duty cycle has been correctly changed the variable $i$ is checked in the outer loop to determine if the amplifier is again in its power supply setting mode which signals the completion of the amplifier adjustment task.

The third conditional comparison checks for both variables Servflg being 'false' and Modflg being 'true'. This condition indicates that no timer generated interrupt has occurred and that a power-on mode of operation is in existence. Thus, the procedure Pwrrpt is called to report the current power supply's forward and reflected powers to the HP microcomputer screen. The relatively low frequency of occurrence of the other tasks handled by this controller strategy allows the repetition of Pwrrpt at such a high frequency that power reporting appears continuous except during the thermocouple reading and temperature display routines.
The final four conditional comparisons (see figure 21), like the second in the control scheme, check both Servflg and another boolean variable. The checking of Servflg prevents the delay of the tasks required after a clock generated interrupt and the other boolean variable signals the request by user for changing a program parameter. The variables Primod, Tcpflg, Tempchng, and Controlno are set 'true' when it is desired to toggle the manual/feedback control mode, toggle a thermocouple on or off, change the target temperature and change the controlling thermocouple respectively. Each block of code executed on the proper 'true' testing conditional requests a value or number through text written to the screen, performs the particular change, and writes the changes to the screen. The code executed when toggling from manual to feedback control also sets the variable Bumpless equal to 'true', signaling the power adjustment code of this condition.

Another control scheme is implemented in program CONTROL_2. This program utilizes the duty cycle of the Wavetek function generator instead of the URI Therm-X duty cycle values to control output power. This control scheme operates identically to the scheme of program CONTROL_1 (see figure 21) except that the controller calculations and power adjustment routines are replaced with a block of code flowcharted in figure 25.

After detecting the boolean variables Chngamp and Power as being 'true', another conditional test is made to determine if the boolean variable Bumpless is 'true'. If Bumpless is 'true', the procedure Ampchk is called to determine the setting of the URI
Figure 25  Flowchart: Controller and Power Adjustment Routine of Control 2 Controller Scheme
Therm-X power amplifier. The power is then turned off via an output disable command being sent to the Wavetek function generator whose output is used as a reference input to the amplifier unit. The average duty cycle value returned from procedure Ampchk is then used as the input to the Wavetek duty cycle changing segment of this code. The URI Therm-X is then set to a duty cycle of one on all channels. The unity duty cycles are then stored, the amplifier is placed in its power supply reporting mode, and sufficient delays and element resets are used to clear the amplifier interface. Then the URI Therm-X duty cycle values are changed in the amplifier itself. The new values of duty cycles are then printed to the screen.

In the event that Bumpless was not set 'true', the routine operates as though control is desired and control has been effected since at least the last temperature reading interval. At this point the same control calculation and adjustment of the calculated change which is used in program CONTROL_1 is used to determine the new adjustment in power.

After the either bumpless transfer or normal control calculations have been finished, the calculated change is added to the duty cycle storage variable, the duty cycle value is converted to a character string compatible with the Wavetek signal generator's communication protocol and the character string, along with proper introduction and termination characters, is sent to the signal generator effectively changing the active duty cycle.
Another difference between this and the first control scheme is that an eighth conditional has been added to the seven major conditionals. This conditional works in the same manner as the final four conditionals in the first control scheme and allows the operator to interactively change the gains used in the control algorithm.
CHAPTER 3
EXPERIMENTS IN TEMPERATURE CONTROL

3.1 IN-VITRO CONTROL EXPERIMENTS

3.1.1 In-Vitro Equipment and Procedures

In the interest of examining the effect of changes in system constraints on the quality of control obtained with the system using any of various control schemes, it was necessary to bridge the gap between the therapy transducers and temperature measuring thermocouples with some form of perfused medium. As perfused ultrasound phantoms are necessarily difficult to construct and maintain, a perfused model using a preserved organ was used instead, providing the advantage of controlled perfusion and preservability. The target tissue mass was obtained and preserved in accordance with procedures ensuring its integrity [20]. Extensive tests were performed relating the effects of changing an integral controller gain at differing levels of perfusion. The effects of moving the scan path off the thermocouple location, increasing the maximum power supply value, and implementation of a "derivative" term in the controller scheme were tested to a limited extent.

The target tissue was affixed to the bottom of a hollow lucite cube of volume 10.65 liters which was placed on the plastic membrane of the Octoson® imager (figure 26). The bottom plate of the cube contained a small window of mylar membrane to allow the passage of
Figure 26 Experimental Setup For In-Vitro Control Experiments
ultrasonic energy into the cube's interior. The mylar window and the Octoson's® plastic membrane were sonically coupled with a commercially prepared sonic transmission gel.

The cube was then filled with a solution of ninety percent alcohol and ten percent water. This solution was continually drawn through a degassing system to remove dissolved gasses and pumped through a thermal energy exchanger suspended in the Octoson's® water tank to help maintain a constant temperature. The input and output ports of this environmental stabilization system were placed at opposing corners of the lucite cube to ensure adequate flow over the target tissue.

The tissue mass itself was perfused with the environmental fluid through the use of a separate peristaltic perfusion pump. The output port of this pump was connected to both a pressure monitor and the renal artery. The pressure measured was maintained below that of an active artery and the volume rate of perfusion was controlled by the speed of the perfusion pump.

The rate of flow was controlled to values of 0, 5, 14, and 20 milliliters per minute of alcohol-water mixture supplied to the entire tissue mass. The rate of perfusion was measured by timing the flow into a graduated cylinder before and after each experimental run, and adjusting the speed of the perfusion pump accordingly. Maintenance of flow rate during the experimental runs involved checking for changes in pressure in the system using the pressure monitor but this concern was not a factor as the perfusion system was inherently stable.
A single thermocouple probe was used within the target tissue and it was that probe's end thermocouple junction which was used in the control experiments. The junction of interest was placed approximately two millimeters below the upper surface of the kidney in the interest of controlling the temperature in a region of high perfusion (figure 27). The remainder of the junctions in the probe served to indicate the temperatures of the adjacent target tissue and of the alcohol bath in which the tissue was submerged.

The speed and periodicity of the scan were representative of an attempted treatment in which a thermocouple to be controlled might be placed at the edge of a two centimeter diameter tumor. The scanning pattern chosen for the experiments was such that the focus of the therapy transducer traveled in a periodic fashion (back and forth) in a straight line through the location of the controlling thermocouple and terminated at each end outside of the tissue volume. The speed of travel of the focus and the amount of time spent in a pause at each end of the scanning path were adjustable, allowing variability of both the scanning speed and scanning period. The scanning pattern chosen consisted of the linear scan with a length of fifty millimeters. The end delay was chosen such that, at a scanning speed of thirty millimeters per second, the period between successive passes of the focus through the thermocouple location was 4.2 seconds.

The controller itself adjusted only the reference duty cycle value, so a maximum power supply value was chosen before the first
Figure 27  Location of Thermocouple Junction Within Target Tissue
experimental run to ensure that the target temperature would be attained at the highest perfusion value used.

Each experimental run was started with the temperature of the tissue between 32° C and 33° C (the temperature of the Octoson® water bath) and the target temperature chosen for the controller was 39° C. These values represent a 6.5° ± 0.5 centigrade temperature elevation, which adequately represented a temperature rise from 37° C (body temperature) to 45° C (0.5 degrees above what is currently considered therapeutic). Data for each experimental run was gathered for a total of 12 minutes. The first 10 minutes were a period of heating and temperature control. The final 2 minutes recorded the thermal decay after the end of a heating segment. Data sampling occurred at 15 second intervals in all experimental runs, and the starting position of the scanning pattern was not correlated with the data sampling (i.e.: control tests started at random points in time while the scanning mechanism ran continuously). During the entire heating interval the environmental fluid was maintained at the temperature of the water bath simulating the relatively stable condition of lower body temperature in tissues surrounding the target mass.

The described experimental configuration along with the capabilities of the previously described scanned focussed ultrasound hyperthermia system and software were sufficiently capable of allowing the investigation of the quality of single point control obtainable.
3.1.2 In-Vitro Tests And Results

A set of thirty-five twenty-two minute controlled treatments were performed in one kidney at four perfusion values: 0, 5, 14, and 20 milliliters per minute, and at seven different integral gains: 1, 3, 5, 7, 10, 15, 20. Three typical experimental data graphs are shown in figure 28. These graphs represent experiments run at the fourteen milliliter per minute flow value, but the general form and trends of the temperature trajectories appear similar for the varying gains at the other tested flow values. A digital interpretation of the applied power appears along the bottom of each graph and the graph itself represents the controlled thermocouple temperature trajectory during the experiments plotted with respect to time.

The temperature data gathered was evaluated using a computer algorithm which calculated the times from the start to reaching the targeted temperature, percent overshoot values, steady-state fluctuation magnitudes, and the frequencies of the steady-state fluctuations. These values were then plotted against a change in the integral controller's gain for each perfusion value (figures 29-32).

The time to target temperature was calculated by noting the first temperature measurement which appeared above the target temperature and, using that value and the previous temperature reading, a linear interpolation was performed to determine the time at which the temperature trajectory attained the target temperature.
Figure 28  Typical Experimental Data At Three Gains
Figure 29  In-Vitro Results: Time To Target Temperature Vs Gain

Figure 30  In-Vitro Results: Percent Overshoot Vs Gain
Figure 31  In-Vitro Results: Magnitude Of Steady-State Fluctuations Vs Gain

Figure 32  In-Vitro Results: Frequency Of Steady-State Fluctuations Vs Gain
The percent overshoot was determined as the difference between the first detected peak (local maxima) temperature and the targeted temperature divided by the difference between the targeted temperature and the starting temperature.

The steady state fluctuation magnitudes and frequencies were evaluated using a peak detection routine. The peak detection routine searched the data backwards from the last recorded temperature to the first recorded temperature. All peaks (local maxima after reaching the targeted temperature) and troughs (local minima) were located and the last and first of these peaks and troughs excluded from the calculation of any steady-state characteristic. The routine also required a minimum of four peaks and three troughs to be present in the remaining data before allowing the calculation of any steady-state characteristics.

The steady state fluctuation magnitudes were calculated by averaging all the peak temperatures and then averaging all the trough temperatures. The fluctuation magnitude was then taken to be the difference between the average peak and average trough temperatures.

The frequency of the steady state fluctuations was determined by noting the time between the first and last valid peaks and the number of troughs occurring during that period. The frequency was then determined as being the number of troughs divided by that duration of time.

The first graph of figure 28 was obtained using a relatively low gain. This low gain resulted in an initial change in power being calculated which did not cause the the applied power to be at
saturation during the first heating interval. This effect caused greatly increased times to target temperature at gain values lower than those used in these experiments (results not shown). At a medium gain, as in the second graph of figure 28, and at a high gain, as in the third graph of figure 28, the power output was at saturation and the times to target temperature remained relatively constant for those gains. A notable exception to this general trend was that at the highest perfusion rate, a large variation in time to target temperature occurred. This was due to the effects of both the relatively moderate slope of the temperature trajectories and the superimposed fluctuations due to the scanning of the power focus leading to a wide variation in times at which the targeted temperature was achieved. The times to target temperature were generally increased with an increase in the perfusion (figure 29).

The first graph of figure 28 also shows the slow response in the plot of the power output obtained at the lower gain values. After target temperature was achieved, the relatively low calculated change only slowly reduced the power and allowed a large overshoot to occur. This effect was reduced at higher gains due to the more aggressive adjustment of power. The lower overshoots at higher gains are also evidenced in figure 30, except at the 0 milliliter per minute flow rate where the passing of the scanning power focus near the thermocouple around the time of the temperature reading has caused greater fluctuations in the data. It is also shown there that a decrease in perfusion caused a higher overshoot and this was due to
the faster rise in the temperature trajectory and the systems relatively slow sampling speed.

The third graph of figure 28 shows a prominent characteristic obtained in the typical high gain experiments. That characteristic was an increased magnitude of the steady-state fluctuations. The increased gain resulted in a more aggressive change in power at each reading interval and is evidenced in the power plot of the graph. Figure 31 shows the effect at all perfusion values and suggests that the magnitude of steady-state fluctuations has little dependence on the perfusion rate for the perfusion values used in these studies. In the case where conduction was the only mode of energy dispersal (flow at 0 ml/min) the fluctuations increased dramatically.

At low gains the frequencies of the steady-state fluctuations at all blood flows were grouped and very low (approx. 0.011 Hz). This dominant frequency, evident in the low gain graph of figure 28, was due to the timing between the scanning focus location and the data sampling period. As gain increased, the frequency increased due to the more aggressive effect of the controller which changed the rate of the temperature fluctuations. This continued with increasing gains until a value limited by the sampling period (15 sec.) was approached (0.033 Hz). At low perfusion rates (figure 32) the frequency of the steady-state fluctuations began to decrease with increasing gain. This effect was due to the slower decay from higher temperatures (i.e.: longer decays through many reading intervals) and a correspondingly lower number of changes in the sign of the slope of the temperature trajectories.
3.2 IN-VIVO CONTROL EXPERIMENTS

3.2.1 In-Vivo Equipment And Procedures

The described scanned focused ultrasound hyperthermia system and software were tested with two separate in-vivo tissue masses. One set of data was obtained from the use of an anaesthetized dog's thigh muscle as a target tissue mass, and another set was obtained from the use of an anaesthetized dog's kidney as a target tissue mass. The thigh experiments provided a means to test the controller in a more homogeneous (all muscle) tissue mass and examine its behavior in a "best case" situation. The in-vivo kidney experiments were done to test the controller's effectiveness in a region of tissue containing areas of both high (renal cortex) and low (renal medulla) perfusion. The kidney provided a good model for some tumors as both the highly perfused outer tissue and necrotic tumor core were simulated.

In the in-vivo thigh experiments, an anaesthetized dog was placed on the Octoson® membrane in such a fashion that its thigh muscles were in the scanning region of the therapeutic ultrasound transducers (figure 33a). The two thigh muscles were sonically coupled with a commercially produced ultrasonic gel. Eight seven-sensor thermocouple probes were placed into the two thigh muscles. The probes were aligned in a vertical plane with a spacing of approximately one centimeter. The dimensions of the entire field of thermocouples were seven centimeters high by six centimeters deep. The scanning pattern used was a two centimeter diameter octagon
Figure 33  Experimental Setup for In-Vivo Control Experiments
in a horizontal plane approximately three centimeters deep within the tissue, and at approximately the elevation of the third thermocouple probe from the bottom. The exact location of the scan with respect to the thermocouple field was not determined as only the effect of the heating needed to be present at one thermocouple junction to effect the control.

The kidney experimental setup utilized a previously described in-vivo kidney model [21]. The model is implemented by surgically installing both an ultrasonic fluid flow meter and a pneumatic arterial occluder on the renal artery which supplies blood to the kidney. This installation allows the perfusion of the kidney to be both measured and controlled. The animal was then placed on the Octoson® membrane to allow directing of the energy from the therapy transducers into the prepared kidney and scanning in the region of controlled perfusion. The thermocouples were placed into the target tissue as shown in figure 33b. Five of the seven-sensor probes were placed in the horizontal plane of the kidney. The spacing between the probes was approximately 1.5 centimeters and the plane of the probes was approximately five centimeters deep within the tissue and above the Octoson® membrane. Three of the seven-sensor probes were placed in the near and far field regions. The scan pattern was a two centimeter diameter octagon in the horizontal plane of the first five probes and the kidney. In this application as with the thigh experiments only the effect of the heating needed to be present at one of the thermocouple junctions to effect the control.
As in all control experiments, the set maximum power supply value was chosen for both thigh and kidney experiments to be that which would allow the target temperature to be reached at the highest perfusion value expected.

The rate of perfusion in the thigh experiments was not controlled but was expected to change during the experiments due to a heat induced vasodilation [11]. The kidney perfusion was controlled during the experiment by observation of the kidney's rate of perfusion on the ultrasonic flow meter and adjustment of the pressure in the arterial occluder.

Each experimental run was started with the temperature of the tissue at the animals resting body temperature which was in the neighborhood of 37° ± 1 C. The target temperature chosen for the controller was 43° C which adequately represented the conditions encountered during hyperthermia cancer therapy. Data for each experimental run was gathered by reading each thermocouple junction every fifteen seconds for a total of twenty-two minutes. The first twenty minutes were a period of heating and temperature control. The final two minutes recorded the thermal decay after the end of a heating segment.

The highest temperature measured in the entire field of thermocouples was used as the control algorithm's input temperature. This strategy was chosen for reasons of safety to prevent to tissues not in the region for which the therapeutic treatment is intended.
3.2.2 Experimental Tests And Results

A set of eight twenty-two minute controlled experiments was performed using the thigh as a target and the tests were run at six different gain values. The controlled thermocouple was that which displayed the highest measured temperature and the controller gain used was the same for more than one experiment to show repeatability of results. A set of five twenty-two minute controlled experiments was performed using the kidney as a target and the tests were run at two different gain values also controlling the highest measured temperature. Experiments with the kidney setup also included a test with a controlled change in perfusion and a test where control was assigned to a single thermocouple.

Figure 34 shows typical thigh data obtained at two gain values. The experiments were run using gains in the low and medium ranges discussed in section 3.1.2. In both cases the average steady-state temperatures measured on the controlled thermocouples were equal to the target temperature.

The lower gain experiment demonstrated both a short time to target temperature and a large overshoot typical of the low perfusion in-vitro experiments, and exhibited both the relatively low magnitude and frequency of steady state fluctuations typical of the low gain experiments in both the in-vitro and the in-vivo studies.

The higher (medium range) gain experiment exhibited a lower overshoot and lower magnitudes of the steady-state fluctuations plus the higher frequencies of the steady-state fluctuations associated with the medium range gain experiments discussed in section 3.1.2. Also
Figure 34 Typical Experimental Thigh Data
evidenced in this test was that the controlled thermocouple was in a region of relatively lower perfusion as demonstrated by the relatively short time to target temperature.

The experiments both showed that control over the highest measured temperature caused the rest of the field of thermocouples to reach steady state values within an approximate ± 0.5°C envelope, and to fluctuate with the same frequencies (0.011 and 0.017 Hz) as the controlled thermocouples. These frequencies were due to both the periodic change in power supplied to the tissue and the periodic nature of the applied power due to the scanning of the power focus. The remainder of the thigh experiments show similar results for moderate adjustments in the integral gain (results not shown).

Figure 35 shows typical results obtained from the kidney experiments. The first graph shows the effect of the controller compensating for a change in perfusion during a medium range gain experiment. The maximum arterial flow rate (200 ml/min) was reduced to no flow (0 ml/min) at the five minute time interval. The change of control to a different thermocouple, caused by the changing perfusion, is evidenced by the data at the six minute time interval.

The second graph of figure 35 shows typical results obtained when control was assigned to a particular thermocouple junction and a very low gain value was used. The slow nature of the low gain integral controller caused typical characteristics of large overshoot and large magnitude of steady-state fluctuations. Superimposed on the low frequency fluctuations and evident in the entire field is a higher frequency fluctuation due to the scanning of the power focus.
Figure 35  Typical Experimental Kidney Data
The response of the entire field of thermocouples followed that of the controlled thermocouple as evidenced in the medium range gain experiment due to the adjustment of power supplied to the target tissue.
CHAPTER 4
DISCUSSION

The trackball data transfer circuitry and software were implemented in the interest of storing enough data from the Octoson® serial section scans to reconstruct significant tissue volumes and effect treatment planning. This implementation was designed to be a means for transferring image data prior to the installation of an IEEE 488 standard interface bus in the Octoson® circuitry allowing communication with the Hewlett Packard microcomputer. The circuitry simply traps the trackball data before it is input to the Octoson® processing circuitry and sends it to the H-P interface. As the Microcomputer and the imager circuitry are not synchronized, the operation of the trackball at a high rate of speed could cause data to be sent to the microcomputer which is not interpreted, due to the imager's lower clock speed, in the Octoson's circuitry. This shortcoming would cause discrepancies between what data is perceived to be collected and what data is actually collected. Avoidance of this problem is attained by noting that a slower operation of the trackball is necessary. After completion of this circuitry, the interface description and software was given to another student to implement a treatment planning software package.

The URI Therm-X amplifier communication software and circuitry were designed to carry out control functions by allowing the adjustment
of the different channel's duty cycle settings and the power supply voltage from the H-P microcomputer. The amplifier is controlled through a serial interface through which character data is sent. Upon sending each character from the microcomputer a delay is necessary to allow the amp's processing and to receive a corresponding status message. This send-and-wait protocol is necessarily slow and, along with the large duty cycle step constraint (one-sixteenth of the maximum), sufficiently degrades the quality of control to the point where large temperature fluctuations (+ 2° C) are induced in the target tissue. That type of control scheme (implemented in program Control_1) is of limited use. This limitation is overcome by the use of the Wavetek signal generator as an input source to the amplifier, allowing the adjustment of duty cycle by steps of one ten-thousandth of full duty cycle (implemented in program Control_2). The modular form of the program used to implement the various control schemes (Control_1 and Control_2) resulted in a set of software which is easily interpreted, user friendly, and can be used as both an experimental laboratory tool and as a means for the clinical application of this type of cancer therapy.

Results of the in-vitro control experiments demonstrated the programs effectiveness and showed that the particular control algorithm used can provide adequate control over the temperature recorded at a thermocouple placed in a target tissue mass.

An important consideration is that before each experiment (or treatment) is started, each of the limiting constraints had to be considered to account for its effect on the quality of control
obtained. The greatest effects noted during the experiments were due to the maximum power supply setting, the scanning pattern characteristics, and the selection of the integral controller gain.

The first constraint resulted from the control calculation providing a change in duty cycle which represents a percentage of the amplifier's maximum power setting. That maximum power must have been sufficient to drive the temperature to above the targeted temperature before any control could occur. Therefore, it was necessary to judiciously choose that setting before the experiments. For example, too low of a maximum power would lead to an infinite time to target temperature at higher perfusion values, or an increase in perfusion during a treatment could cause previously controlled temperatures to eventually fail to maintain the target temperature. Changing the maximum power supply value also effectively changed the gain of the controller by directly effecting the output represented by each duty cycle value (eq. 3, sec. 2.5.2). A choice of too high a maximum power would have the effect of using too high a gain value and adversely effect the quality of control through increased magnitudes of the steady-state fluctuations.

The second set of constraints which had to be considered, the scanning characteristics, were a function of both the proximity of the scanning path to the thermocouple junction and the periodicity of the scanning. These constraints were affected by the choice of scan pattern and speed of the scanning focus before the experiments. Obviously, the power deposition must have affected a thermocouple's temperature to allow control over that temperature. That is, between
changes in power, the scanned focus must have passed within the neighborhood of the junction and caused a change in temperature for the corresponding control calculations to have been effective. The importance of these parameters was evident in the experimental data, such as in the spread of times to target temperature at higher perfusion values, the spread of percent overshoot values at lower perfusions, and the grouping effect of the fluctuation frequencies at lower gains, all discussed in sec. 3.1.2.

The third important parameter and the independent variable in the in-vitro studies was the chosen gain. In defining a set of good control characteristics in hyperthermia one would hope to achieve a short time to target temperature, a low percent overshoot and a low magnitude of steady-state fluctuations. The data obtained in the in-vitro experiments shows little correlation between gain and time to target temperature. It is noted that a higher gain resulted in a lower overshoot due to the more aggressive controller's changing the temperature trajectory's slope from a positive to a negative value at an earlier sampling interval (figure 30), but the higher gains resulted in an increased magnitude of steady-state fluctuations (figure 31). The reason for this effect was evidenced in the frequency of steady-state fluctuations (figure 32). As gain was increased, the frequency of fluctuations also increased. Near a particular "threshold" gain (between gains 5 and 7 in the data) the frequency of the fluctuations tended to either level or decrease with increasing gain. The upper limit on the frequency was set by the sampling period itself, and occurred when the gain was high.
enough to effectively change the sign of the trajectory slope at each sampling interval. In the data sampled at fifteen second intervals, the highest possible recorded fluctuation frequency is 0.0333 Hz and is evident in the high gain plot of figure 28. At values above this "threshold" gain the increase in gain only served to increase the magnitude of the steady-state fluctuations.

In light of the above discussion it was apparent that the best control achieved was within a band of gains below the described "threshold" gain and above a gain which caused excessive overshoot. This band of gains provided the control characteristics of an overshoot temperature near that of the upper limit of the peaks of the steady-state fluctuations and a steady-state fluctuation frequency somewhat below that which appears as the upper limit due to the sampling characteristics. The data gathered shows this band of integral gains to be between 5 and 10 for the specific in-vitro experimental setup. Those gain values avoided both the high overshoot values typical of low gain integral controllers and the increased magnitude of steady state fluctuations of the higher gain experimental runs (figures 29-32). A good example of this result is the medium range gain graph of figure 28 in which the gain used was 5 and the flow rate was 14 milliliters per minute.
CHAPTER 5
CONCLUSIONS AND RECOMMENDATIONS

The described control system for a scanned focussed ultrasound hyperthermia cancer therapy system has been shown to be effective in the control of the temperature of the target tissue in simulated treatment experiments. It was shown that if the system is used with the integral control algorithm tested, a range of controller gains can be found which provide the desired low overshoot, provide low magnitude of steady-state fluctuations, and make the controller response quite robust with respect to changes in perfusion. This band of gains is also quite wide provided the amplifier's maximum power setting is adjusted within a range which will just allow the maintainence of the targeted temperature at the highest perfusion levels encountered during the experiment or treatment, and which still provides a power margin for controlling adjustments.

It should be noted that a great improvement on the quality of control could be attained by both increasing the sampling and power adjusting frequency and increasing the speed of the scanning power focus. These two parameters are currently the limiting factors on the equipment used in this investigation. The slower scanning speeds enhance the temperature fluctuations caused by the passing power focus [9]. The power is turned off for a finite interval of time before the reading of the thermocouples to allow the resultant temperature spikes to decay to the temperature of the
surrounding tissue. This power-off interval produces a limit on the allowable sampling frequency due to the resultant duration of the power-on intervals. A higher scan speed would reduce these fluctuation magnitudes allowing shorter power-off intervals, longer power-on intervals, increased sampling frequencies, and greatly increased control quality.

The effectiveness of the integral control algorithm tested and demonstrated in the in-vitro and in-vivo studies invites its use in the clinical environment and its development in a more complex controller scheme. The statistical evaluations of the data during a treatment might be used in an adaptive control scheme to allow on-line adjustment of the controller gain. An examination of the time to target temperature, overshoot, and fluctuation frequency would be used to adjust the controller gain and optimize the quality of the control obtained. In this way, operation in the described band of gains providing good control could be maintained.

A simple extension of this control scheme is the implementation of a multipoint control algorithm in which a number of thermocouple junctions are controlled by the adjustment of power as a function of position of the scanned power focus [22]. The path of the scanning focus is considered equivalent to a number of short linear segments, like the one used in the in-vitro studies, and the controlled thermocouples adjacent to the scan segments are used as the controlling temperature inputs. This scheme operates on the assumption that the system is a weakly connected distributed parameter system (i.e.: conduction of thermal energy between segments is low). In the event
that the temperature field is uniformly elevated to the targeted
temperature this assumption is valid, and control strategies such
as the one implemented in the experiments can be used to control
many thermocouples in the multipoint control scheme described.

Although the capabilities of the amplifier are not sufficient
to effect a high quality control without the use of a separate
signal generator, the described communication link will no doubt
play an important role in future implementations of adaptive and
rule governed control schemes. For example, when a particular
temperature trajectory fails to reach a targeted temperature, the
HP/URI Therm-X communication link may be used to increase
the amplifier's maximum output power. Adjustment of the amplifier's
individual channels may be found necessary in future control schemes
and can also be affected through this link.

The trackball/HP communication link is, at the time of this
writing, being used in the development of treatment planning
software. Its function will be to provide basic data used to
determine the discussed scan pattern characteristics which would be
optimal in the individual treatments, and its effectiveness in this
endeavor looks promising.

In conclusion, it has been shown that the described control
scheme has been successfully implemented and shown to be effective
in obtaining good control over temperatures obtained during the
application of scanned focussed ultrasonic energy in hyperthermia
treatments, and the overall control system also provides a convenient
base for further study into this unique problem in control.
REFERENCES


