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A Multifrequency Driving System for Ultrasound Hyperthermia

Combining Power Patterns of Different Frequencies for Improved Tumor Therapy

Hyperthermia (the heating of tumor cells) is a type of adjuvant cancer therapy. In previous studies, heating tissues to temperatures above 42°C has been shown to destroy cells as well as augment the effects of cancer therapy such as radiotherapy and chemotherapy [1-4]. Ogilvie, et al. [5], indicated that current techniques and equipment using microwave and radio-frequency energies appear to produce largely inadequate heating patterns in superficial or accessible tumors and in normal tissues. In place of electromagnetic energy, ultrasound techniques have shown promise for delivering controlled heating of both superficial and deep lesions.

Ultrasound phased arrays using electrically programmable synthesis of focal size, shape, and position can offer a flexible heating method. Several types of ultrasound phased arrays with a single operating frequency have been proposed for hyperthermic purposes [6-12]. Moros, et al. [13], pointed out that the lateral conformability of power deposition is improved by a dual-frequency system. Their results showed that by varying the power outputs from the low- and high-frequency arrays, the depth of the 50% isopower contour can be controlled over a range of 3 cm. The depth of therapeutic isotherms over a 2.5 cm range is controlled by different low-to-high power ratios. Lin, et al. [14], demonstrated that the combination of low and high frequencies can be used to obtain a therapeutic range covering the breast with a more uniform specific absorption ratio (SAR) ratio. Lalonde and Hunt [15-16] used field-conjugate lenses with a variable-frequency driving signal (0.75 to 2.6 MHz) to achieve focus scanning. They indicated that field-conjugate lenses have the advantage that their focus patterns are frequency dependent.

Compared with a single-frequency system, the multiple-frequency system has an additional function to combine power patterns of different frequencies.

This function increases the availability of power patterns to treat various shapes and depths of tumors. Therefore, we proposed a system with the ability to drive ultrasonic phased arrays of multiple resonant frequencies for ultrasound hyperthermia, which will be discussed in this article.

Materials and Methods

System Architecture

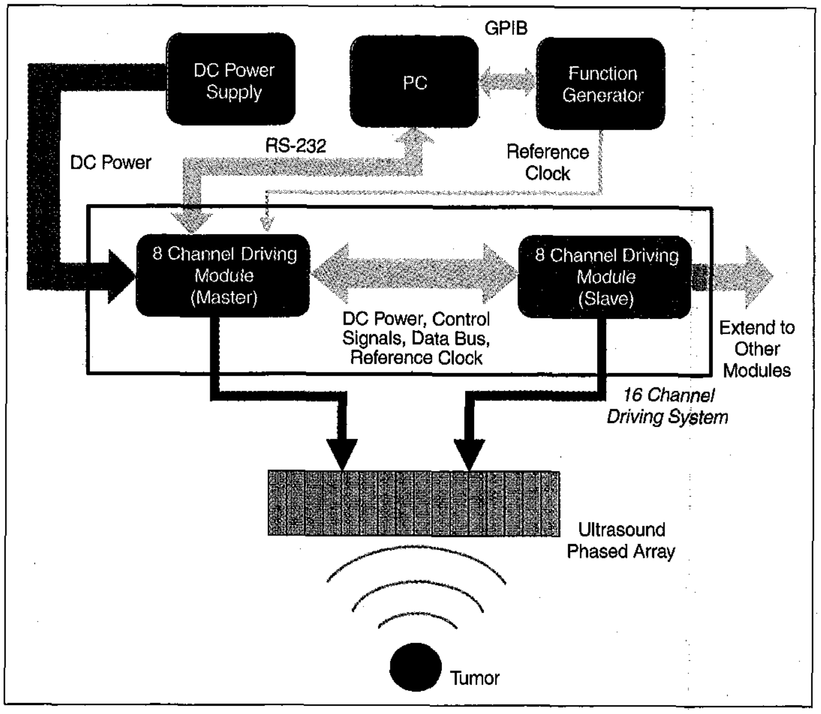
The architecture of this hyperthermia system is depicted in Fig. 1. There are two driving modules—the master module and the slave. Each driving module contains one main board and eight driving cards. The power source supplies DC voltages of +64 V, +12 V, −12 V, and +5 V. The reference clock of the driving system is generated from the synthesized function generator (Model: DS345, Stanford Research Systems, Sunnyvale, CA). Using the RS-232 communication protocol, the PC can individually control the output power level and relative phase of each channel by transmitting instructions to the driving system.

Main Board

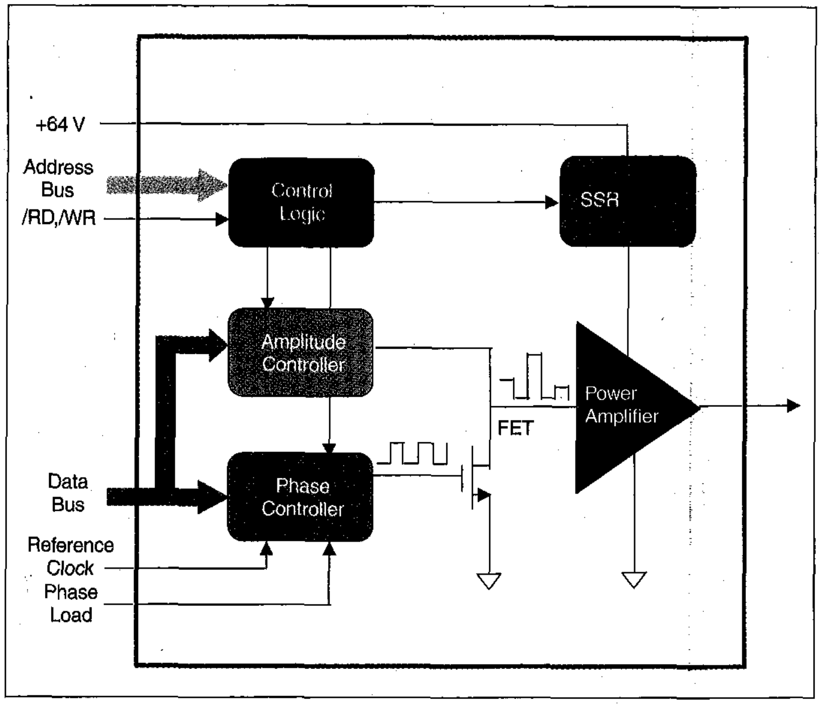
The main board is composed of one microprocessor (AMTEL 89C51), three parallel ports, and nine slots for plug-in driving cards. The parallel ports contain power lines, control lines, data bus, address bus, and reference clock to connect with the main board in the other module. There are two operation modes in the main board. In the master mode, the microprocessor receives instructions from the serial port and controls the driving cards. In the slave mode, the microprocessor must be detached from the main board so that the master main board can control the slave main boards by the connection of parallel ports.

Driving Cards

The block diagram of the ultrasound driving cards is shown in Fig. 2. The driving card is inserted in the slots on the main board with 62 golden fingers. Each driving card includes four units: phase shifter, amplitude controller, power amplifier, and on-off switch. The programmable electrical erasable logic (PEEL) (ICT-22CV10) device, programmed as an n-bit ($1 \le n \le 8$, here $n = 4$) preloadable counter, serves as a 2^n frequency divider with a 2^n-step phase-shift function. The reference clock runs at 2^n times that of the transducers' driving frequencies and inputs the pin designated as "CLK_IN" in the PEEL. Then, the initial values of the n-bit counters in the 16 channels are individually preloaded by instructions from the PC. The counters are triggered by the same signal to the input pin ("LOAD") and count the reference clock simultaneously. Due to the different preloaded initial values, the output voltage levels of the counters change at different time points. Therefore, the output relative phases of the counters can be controlled by the preloaded initial values from the PC to obtain the phase-shifted square waves with the resonant frequency of the



1. Block diagram of the driving system for ultrasound hyperthermia.



2. Block diagram of the driving cards.

Because of its broad bandwidth, this system can concurrently drive transducers of multiple frequencies.

ultrasound transducer. Here, we emphasized that the PEEL device can be easily programmed for different bit counters to individually divide the frequency of the same reference clock for concurrently driving different operating frequencies of the ultrasound transducers.

The aforementioned phase-shifted square wave inputs to the gate of the FET. The voltage of the FET drain depends on the digital input of the digital-to-analog converter (AD7524). The output signal of the FET, serving as the input to the power amplifier, is adjusted for the relative phase and amplitude by the counter and amplitude controller. In this manner, the PC can control the output parameters of each channel.

The power amplifier comprises three stages: preamplifier, push-pull amplifier, and class A power amplifier. In the preamplifier, the square wave from the FET output is filtered to become a sine wave by an RC low-pass filter. The filtered sine wave inputs to the base of a 2N3904 transistor that operates in a common emitter configuration. 2N2219 and 2N2905 transistors serve as a push-pull amplifier to support sufficient input current for the next stage. The output stage is constructed with a pair of RF power MOSFETs (IRF 450) with a transformer of 3:2 coupling. This transformer isolates the connected applicators and ensures electrical safety. A solid-state relay (SSR), used as a power switch for the +64 V power source, is controlled by instructions from the PC to select which channels to turn on or off. If overheating occurs during the hyperthermia treatment, the power switch can be turned off automatically by the PC program.

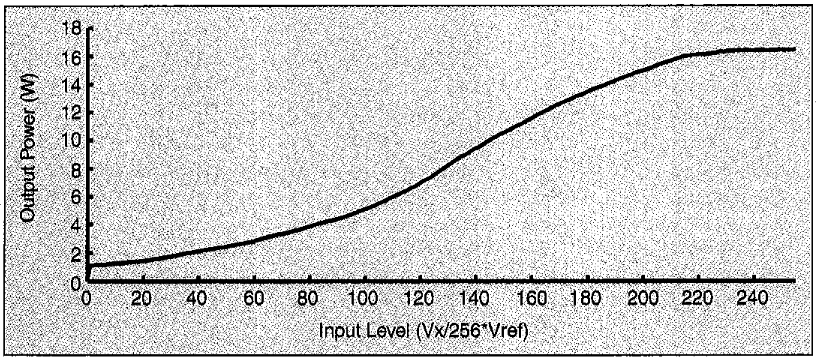
Tests for System Performance

The driving system has been tested for output power with respect to the input amplitude level, power stability, relative phase shifts, and frequency response. The equipment for these tests are a digital power meter (Model: 4421, BIRD, Cleveland, OH) and a digital storage oscilloscope (DSO; Model: 9310A, LeCroy, Geneva, Switzerland). The DSO can present statistics of the real-time stability of measured signals. In these tests, automatic measurement has been realized by a general-purpose interface bus (GPIB) interface. The system is warmed up for at least 10 minutes to achieve thermal steady state before the tests are carried out.

Results

Output Power vs. Input Amplitude Level

For this test, the output of each channel is loaded with a 1.127 MHz, 50 mm diameter disk-type transducer immersed in water. The program in the PC increases the input amplitude level from "0" to "255" every 10 sec. Figure 3 presents the average power output from the 16 channels vs. the input amplitude from the driving cards. The maximum variability of this curve is 1.5 W. This averaged curve can be used to control the output power of each channel.



3. The average of power output vs. input level for the 16 channels.

Power Stability

The PC program maintains the input amplitude level and reads the power from the digital power meter every 10 sec for a total duration of 100 min. The maximum variability of the 16 channels is 1 W (under 10%) during the 100 min of the stability test. This degree of stability ensures that this driving system can used to carry out stable hyperthermia therapy.

Relative Phase Shifts

The maximum phase-shift error for the 16 phase steps in the 16 channels is 10%. The output signals of channel 0 (reference channel) and channel 12 (the channel with the maximum phase-shift error) are shown in Fig. 4. The phase levels transmitted from the PC are 0:0, 0:4, 0:8, and 0:12. The corresponding results are shown in Fig. 4(a), 4(b), 4(c) and 4(d) for the 90-degree phase shift per four phase steps, respectively. Statistical analysis by the DSO shows that, in spite of changing the relative phase, the variances of the output amplitude and frequency are 3.1 V and 0.17 MHz, respectively. Therefore, the output signal is stable.

Frequency Response

In this test, each channel is loaded with a 50 ohm resistor. The input amplitude is held at a constant level while the frequency of the reference clock is varied, yielding the frequency response shown in Fig. 5. Because of its broad bandwidth, this system can concurrently drive transducers of multiple frequencies.

Discussion

This work proposes a multiple-frequency driving system for ultrasound hyperthermia. The ability to drive multiple frequencies concurrently increases the number of power patterns available to treat tumors of various shapes. Lin, et al. [14], showed that the combination of low and high frequencies can be used to obtain a therapeutic range covering with a more uniform SAR ratio. In our system, because the counters of the driving cards are constructed with PLDs, we can easily update the phase resolution and frequency division without any modification of the system circuits. Therefore, this system can concurrently drive transducers of different resonant frequencies so as to improve the power pattern and to control the penetration depth. Moreover, this system can be operated as a single-frequency system to drive transducers of higher frequency to treat superficial tumors or drive transducers of lower frequency for deep-seated tumors.

Most of the circuit devices used in this system operate in a steady state so as to generate stable output signals. On the other hand, the duty-cycle power controller [6-10] continually switches the DC bias, creating an unstable state more frequently than that for the linear power amplifier system. As the impedances of the driving system and the transducer do not match well during the unstable state, power reflecting to the driving system might damage electronic devices and ultrasound transducers in the duty-cycle power control system.

The maximum variation of the average power output for the 16 channels is 1.5 W (Fig. 3). The differences among the 16 channels are attributed to variation of the components on the driving cards. To mitigate this variability, in the PC program we created a look-up table of output power vs. input amplitude level for each channel. This table can be searched to obtain the proper input level to assure the same output power for each channel. Moreover, by selecting driving cards with similar characteristics, we could reduce the differences between channels. Through these techniques, output power differences among the channels can be reduced. Furthermore, by controlling the duty-cycle timing with the PC program to switch the SSRs in the driving cards, the time average power can be controlled in this driving system.

Figure 4 shows the phase shifts of channel 12—the relative phase levels compared to channel 0 are 0:0, 0:4, 0:8 and 0:12, respectively. The relative phase of channel 12 was increased from level 0 to level 15 under the condition of constant input amplitude level. The statistical results show that the measured amplitude and frequency of the output signal have variances of about 3.0 V and 0.017 MHz, respectively. Because the amplitude and frequency of the duty-cycle system are almost zero in the nonduty period, their variance will be much larger when the output is measured by this same method

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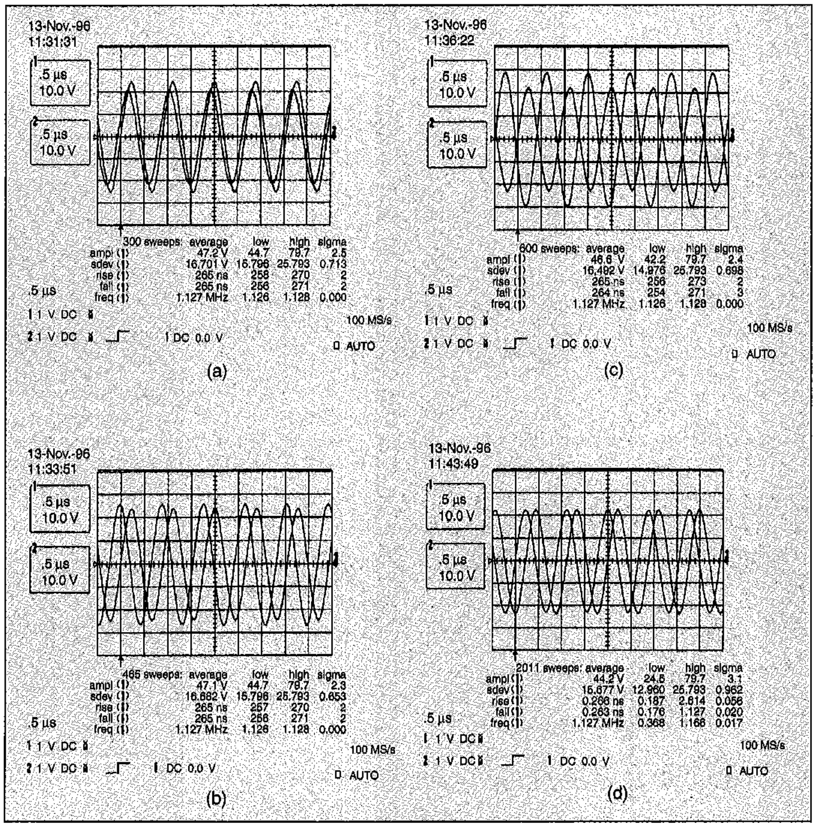


```
300 sweeps: average    low    high  sigma
ampl (1)     47.2 V   44.7    79.7    2.5
sdev (1)   16.701 V 16.796  25.793  0.713
rise (1)     265 ns    258     270      2
fall (1)     265 ns    256     271      2
freq (1)  1.127 MHz  1.126   1.128  0.000
```

(a)

```
465 sweeps: average    low    high  sigma
ampl (1)     47.1 V   44.7    79.7    2.3
sdev (1)   16.682 V 15.796  25.793  0.653
rise (1)     265 ns    257     270      2
fall (1)     265 ns    256     271      2
freq (1)  1.127 MHz  1.126   1.128  0.000
```

(b)

```
600 sweeps: average    low    high  sigma
ampl (1)     46.6 V   42.2    79.7    2.4
sdev (1)   16.492 V 14.976  25.793  0.698
rise (1)     265 ns    256     273      2
fall (1)     264 ns    254     271      3
freq (1)  1.127 MHz  1.126   1.128  0.000
```

(c)

```
2011 sweeps: average    low    high  sigma
ampl (1)      44.2 V   24.8    79.7    3.1
sdev (1)    15.677 V 12.960  25.793  0.962
rise (1)    0.266 ns  0.187   2.614  0.056
fall (1)    0.263 ns  0.176   1.127  0.020
freq (1)   1.127 MHz  0.368   1.168  0.017
```

(d)

4. An illustration of the records for the phase-shift test with relative phase levels of (a) 0:0, (b) 0:4, (c) 0:8, and (d) 0:12, respectively. The statistical values show that the output signal is stable.

The phase-error tolerance depends on the geometric shape of the ultrasonic applicators. Considering the maximum 10% phase-shift error of this system, before treatment it is necessary to evaluate whether such errors are acceptable. The phase resolution of the 4-bit counters in this system is 22.5 degrees; that is, the worst case of phase error is 11.25 degrees. If the 4-bit phase resolution is not acceptable, it is easy to upgrade the phase resolution by erasing and re-programming the counters.

Lalonde and Hunt [15-16] used field-conjugate lenses with a variable-frequency driving signal (0.75 to 2.6 MHz) to achieve focused scanning. Field-conjugate lenses have the advantage that their focus patterns are frequency dependent. Because of the broad bandwidth (Fig. 5), this system can use field-conjugate lenses to drive the transducers. Through the GPIB interface, the PC program can control the frequency of the reference clock from the function generator for focused scanning.

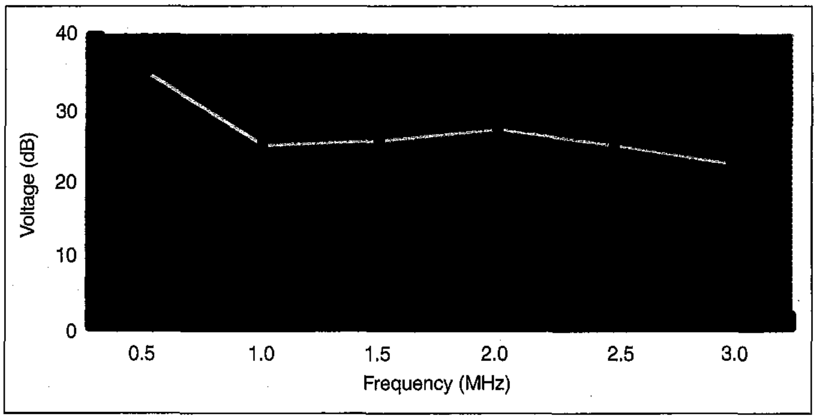
The printed-circuit layout of the driving card is designed to connect the plug-in slots on the main board with the golden fingers on the driving cards. One master module can control multiple slave modules by the connection of parallel ports, and the system can thus be extended module by module.

This driving system can be applied as an adjuvant treatment with other medical therapies.

With this design, it is convenient to extend and maintain the driving system.

Conclusion

Above all, the driving system is able to: (1) drive multi-element applicators or phased arrays of a single resonant frequency through the multichannel linear power amplifiers, (2) concurrently drive transducers with different resonant frequencies, (3) adjust the relative phase and output power of each channel for the scanning ultrasonic focus, and (4) operate each channel with good output stability. This driving system has the flexibility to drive transducers of higher frequency for superficial tumors or lower frequency for the deep-seated tumors. Through the proper design of ultrasound applicators, this driving system can be applied as an adjuvant treatment with other medical therapies.



5. The frequency response of the driving system. Because of a broad bandwidth, this system can concurrently drive transducers with multiple frequencies.

Acknowledgments

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Brain Teaser ANSWERS *(from page 36)*

1. Seven-year-olds do not have wives in Chicago, and fathers rarely confuse their children's names. This type of logic yields Mr. White as president, Mr. Green as professor, Mr. Black as instructor, and Mr. Green as handyman.

2. Frank (winner), Joe, Jane, Tom, Joan.

3. There are five permutations of any five numbers. The probability is thus: 1/5 x 4 x 3 x 2 x 1 = 1/120.