

**Bioelectric Notes**

Note 5

15 March 2010

**Bioelectric Pulses and Electromagnetic Pulse Standards**

Carl E. Baum and Serhat Altunc  
Department of Electrical and Computer Engineering  
University of New Mexico  
Albuquerque, NM 87131

Karl H. Schoenbach and Shu Xiao  
Frank Reidy Research Center for Bioelectrics  
Old Dominion University  
Norfolk, VA 23510

Abstract

*Fast electrical pulses are used to treat skin cancer with positive results. Here we compare such exposure with the standards used for personnel safety. We also consider some alternate exposure techniques in this context.*

\*\* This work was sponsored in part by the Air Force Office of Scientific Research

## 1. Introduction

For some time now, fast pulses have been used to kill skin cancer (melanoma) [1]. These have very large amplitudes ( $\text{MVm}^{-1}$ ) with short pulse widths (ns). However, one may ask what such pulses might do to otherwise-normal nearby tissue (human or test animal).

There is a widely used and respected safety standard for exposure of human beings to electromagnetic fields [2]. This paper explores the use of electromagnetic pulses in the context of the abovementioned use for attacking skin cancer. How close do these pulse exposures come to the safety-standard limits? This is applied to the currently used direct-contact-electrode system, as well as a radiated-pulse system under development.

## 2. Exposure standards

Based on a thermal model of absorbed energy (dose), the IEEE and ANSI have promulgated safety standards for exposure to electromagnetic (EM) radiation [2]. Averaged over a 6 minute time interval (rms), these can be summarized for an “uncontrolled” environment for a plane wave as:

<u>MPE</u>	<u>Frequencies</u>
614 $\text{Vm}^{-1}$	} 3KHz to 3 MHz (low-frequency region)
103 $\text{Wm}^{-2}$	
dropping ( $\propto f^{-1}$ ) to	
61.4 $\text{Vm}^{-1}$	} 30MHz to 300 MHz (resonance region)
10 $\text{Wm}^{-2}$	
rising ( $\propto f^{-1/2}$ ) to	
106 $\text{Vm}^{-1}$	} 3GHz to 300 GHz (high-frequency region)
100 $\text{Wm}^{-2}$	

Table 1. Summary of Maximum Permissible Exposure (MPE) Limits (power density averaged over six minutes)

There are also safety limits established for a single pulse (less than 100 ms width) as:

$$\text{Peak MPE} = [360 \text{ seconds}] \text{ MPE} / 5 [\text{pulse width (seconds)}] \quad (2.1)$$

For a trapezoidal pulse, typical for pulses used in bioelectric studies [1,3,4,5,6] [Fig. 1] the frequency spectrum can be described as [7]:

$$X(f) = \frac{2A}{\tau_r(2\pi f)^2} [\cos\left(2\pi f \frac{\tau}{2}\right) - \cos\left(2\pi f \left(\frac{\tau}{2} + \tau_r\right)\right)] \quad (2.2)$$

Where A is the amplitude of the trapezoidal pulse,  $\tau$  is the duration and  $\tau_r$  is the rise- and fall-time.

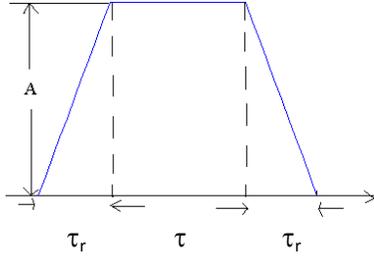


Fig. 1 Trapezoidal pulse as used in bioelectric experiments

For such a pulse the first corner frequency is at

$$f_1 = 1/\pi\tau \quad (2.3)$$

Above this frequency, the envelope decreases with -20dB/decade up to the second corner frequency

$$f_2 = 1/\pi\tau_r \quad (2.4)$$

For higher frequencies, the spectrum decreases with -40dB/decade.

For a subnanosecond-long pulse (FWHM) [5,6] with a rise- and fall-time of 150 ps (ibid.), the second corner frequency is at

$$f_2 = 10^9/0.15\pi = 2.12 \text{ GHz} \quad (2.5)$$

This frequency, which we define as the relevant frequency range for EM radiation effects of subnanosecond pulses, is located right between the resonance region and the high frequency region as described in the previous section.

We consider, therefore, both cases: the case where the safety standards for high frequency (3 GHz – 300 GHz) hold and the case where we are in the resonance region (30 MHz – 300 MHz). Choosing the high frequency range for determining the maximum permissible exposure limit, we obtain using equ. 2.1, for a 1 ns pulse with a risetime of 150 ps:

$$\begin{aligned} \text{Peak MPE} &= 72 \text{ s} (100 \text{ Wm}^{-2}/10^{-9} \text{ s}) \\ &= 7.2 \text{ TWm}^{-2} \end{aligned} \quad (2.6)$$

The power density is given as  $E^2/Z_0$ , with  $Z_0 \approx 377 \Omega \equiv$  wave impedance of free space

Consequently,

$$E \approx 52 \text{ MVm}^{-1} \quad (2.7)$$

which is rather high. This is an order of magnitude above the breakdown field of air ( $3 \text{ MVm}^{-1}$  for “slow” pulses). Choosing the resonance region as the frequency region which determines the maximum permissible exposure limit, we obtain for the same pulse parameters a used before:

$$\text{Peak MPE} = 72 \text{ s} (10 \text{ Wm}^{-2}/10^{-9} \text{ s})$$

$$= 0.72 \text{ TW/m}^2$$

$$E = 16 \text{ MV/m}$$

Although lower than the electric field obtained in the high frequency region, it is still higher by a factor of five than the breakdown field in air (for long pulses).

Of course, one might have the tissue insulated with oil to allow a higher field. In general, however, let us deal with an order of magnitude less fields, or two orders of magnitude less power density. (The standard mentions 100 kV/m peak for pulsed fields, but this is too small for significant therapeutic benefit. This seems to be related to shock hazard, not relevant here.)

Just for a typical number, let us assume a  $3 \text{ MVm}^{-1}$  trapezoidal pulse with 1 ns pulsewidth. Consider multiple (N) pulses (spaced at least 100 ms, or a repetition rate not exceeding  $10 \text{ s}^{-1}$ , from the standard). Then we have, for  $3 \text{ MVm}^{-1}$

$$\text{Power density} = E^2/Z_0 = 24 \text{ GWm}^{-2} \quad (2.8)$$

$$N = 7.2 \text{ TWm}^{-2} / 24 \text{ GWm}^{-2} \approx 300 \text{ pulses (within 6 minutes)}$$

This is an incident field, noting that there is a reflection

$$R = (\epsilon_r^{-1/2} - 1) / (\epsilon_r^{-1/2} + 1) = -.8 \quad (2.9)$$

$$[\epsilon_r = 81 \text{ for water}]$$

at the tissue surface.

### 3. Direct-contact exposure at Old Dominion University

For longer pulses, there is published data [1] with

$$\Delta V \approx 8 \text{ kV (voltage between electrodes)} \quad (3.1)$$

$$\tau \approx 300 \text{ ns (pulse width)}$$

$$\tau_r \approx 30 \text{ ns}$$

The field between two plane-parallel electrodes is for a gap distance of 5 mm (the skin covering the melanoma tumor was pulled up from the mouse and positioned between the two electrodes):

$$E \approx 16 \text{ MVm}^{-1} \quad (3.2)$$

which is about five times the breakdown field strength (for long pulses) in air. In this case, the electric field is a resultant field at the tissue. The equivalent incident electric field is several times (5 times for  $\epsilon_r = 81$ ) larger, for use in comparing to the safety standard.

The second corner frequency for this pulse is

$$f_2 = 10^9 / 30\pi = 10.6 \text{ MHz} \quad (3.3)$$

This frequency is located right between the low-frequency region and the resonance region. We consider therefore again, as in the previous case, both cases:

With these numbers (2.1) gives

$$\text{Peak MPE} = 62 \text{ MPE [Wm}^{-2}\text{]}/ \text{pulse width [ns]} \quad (3.4)$$

for the resonance case:

$$\text{MPE} = 10 \text{ Wm}^{-2} \text{ Peak MPE} \approx 2 \text{ GWm}^{-2}$$

Converting this to electric field (incident) gives

$$E_{\text{MPE}} \approx [(377 \Omega) (2 \text{ GWm}^{-2})]^{1/2} \approx 16.8 \text{ MV/m} \quad (3.5)$$

which is approximately the field that was applied. However, using multiple pulses as it was done in the experiment (1) makes the exposure more severe.

For the low-frequency case:

$$\text{MPE} = 103 \text{ Wm}^{-2}$$

$$\text{Peak MPE} = 20.6 \text{ GWm}^{-2} \quad (3.6)$$

Converting this to electric field (incident) gives

$$E_{\text{MPE}} \approx [(377 \Omega) (20.6 \text{ GWm}^{-2})]^{1/2} \approx 54 \text{ MV/m} \quad (3.7)$$

which is higher than the field that was applied. However, again, since 100 pulses at 0.5 Hz repetition rate were applied, using multiple pulses makes the exposure more severe.

So it appears that the exposure in (3.1) is well above the published exposure standard. Since the electrodes are in direct contact with the melanoma, this is not necessarily a bad thing, since the object is to kill the melanoma. However this raises a question concerning what other types of exposure might be therapeutic without such a severe exposure.

Let us also note that a more refined version of this type of illuminator using coaxial direct-contact geometry [8] may improve things somewhat.

#### 4. Two electrodes straddling target

One might ask if it is possible to straddle the target melanoma with two needle electrodes as in Fig.2. In this case we can estimate the ratio of the fields at the electrodes and the target using a two-dimensional approximation as in [9]. In this case let us choose

$$\begin{aligned} 2b &\approx 6 \text{ mm} \equiv \text{electrode spacing} \\ 2d &\approx .25 \text{ mm} \equiv \text{electrode diameter} \end{aligned} \quad (4.1)$$

The field at the target is

$$E_{\text{center}} = \frac{V}{2[b-d]} f_E$$

where now

$$f_E = \frac{2}{\text{arc cos } h\left(\frac{b}{d}\right)} \frac{\left[\frac{b}{d}-1\right]^{1/2}}{\left[\frac{b}{d}+1\right]} \quad (4.2)$$

$$\approx \frac{2}{\ln\left(2\frac{b}{d}\right)} \frac{\left[\frac{b}{d}-1\right]^{1/2}}{\left[\frac{b}{d}+1\right]}$$

$$\approx .5$$

At the electrodes the field is considerably larger. The relative field is

$$E_{y\text{rel}} \approx \frac{1}{2} \left[ \left[ 1 + \frac{y}{b} \right]^{-1} + \left[ 1 - \frac{y}{b} \right]^{-1} \right]$$

= 1 at center (y = 0)

$$E_{y\text{rel}} = \frac{1}{2} \left[ \left[ 2 - \frac{d}{b} \right]^{-1} + \left[ \frac{d}{b} \right]^{-1} \right]$$

≈ 12 at electrodes

(4.3)

giving an order of magnitude larger field at the electrodes.

This shows the inefficiency of having the electrodes spaced away from the target. Of course, one could have electrodes with the usual Rogowski contours, similar as described in reference 1. This would make the field more uniform, but with very wide electrodes compared to spacing.

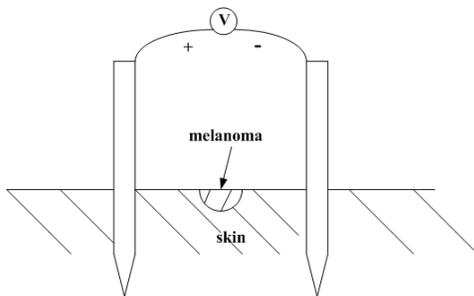


Fig. 2. Direct-contact Pulsed Exposure System

## 5. Advanced radiated exposure at University of New Mexico and Old Dominion University

At the University of New Mexico we are developing a system for later construction and installation at Old Dominion University [10, 11]. This is a radiating system with no electrodes at or near the target. A spherical TEM-wave pulse is launched from one focus of a prolate-spheroidal reflector, and focused at the second focus where the target is located. There will also be a special graded lens going from air to some hit relative dielectric constant (say, 81 for water) in contact with the target.

For some sample calculations let us assume that

$$\begin{aligned}\Delta t &\approx 100 \text{ ps} \\ E_{\max} &\approx 3 \text{ MV/m}\end{aligned}\tag{5.1}$$

This is based on an assumed pulse rise time into the antenna of 100 ps, noting the time derivative that occurs at the second focus. Also the launching pulse is assumed to be a few 100 kV in amplitude. The lens concentrates the beam to a few mm, while increasing the field proportional to  $\epsilon_r^{1/4}$  (i.e., 3 times) [4,5].

Now we have

$$\begin{aligned}\text{MPE} &= 100 \text{ Wm}^{-2} \\ \text{Peak MPE} &= 72 \text{ s} (100 \text{ Wm}^{-2} / 10^{-7} \text{ s}) \\ &= 72 \text{ GWm}^{-2} \\ E &\approx 5.2 \text{ MVm}^{-1}\end{aligned}$$

This electric field is somewhat larger than in (5.1). So, for a single pulse, this exposure is less than the exposure standard. For multiple pulses (within 6 min.) this would be exceeded. However, the exposed tissue is very small in volume (a few mm dimensions), allowing more rapid thermal dissipation, and thus greater exposure in 6 min. [1].

## 6. Concluding remarks

We are in uncharted territory while dealing with fast-pulse fields on biological targets. The exposure standards have some safety margin built into them. When pursuing a therapeutic effect of EM pulse exposure, we need to be cautious, perhaps building up the exposure and noticing both therapeutic and potentially damaging effects. One may wish to use multiple pulses, noting a possible  $N^{1/2}$  dependence for biological efficacy [12,13]. One may be limited in pulse repetition rate if one wishes to use a large number of pulses.

While one may be concerned with deleterious effects with overexposure to EM pulses, still there are demonstrated (on mice) health benefits of appropriate EM exposure. Perhaps, someday, one may wish to take a regular dose of vitamin EM.

## References

1. R. Nuccitelli, U. Pliquett, X. Chen, W. Ford, R.J. Swanson, S.J. Beebe, J.F. Kolb, and K.H. Schoenbach, "Nanosecond Pulsed Electric Fields Cause Melanomas to Self-destruct," *Biochemical and Biophysical Research Communications*, 2006, pp. 351-3
2. "IEEE Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic fields, 3 kHz to 300 GHz," IEEE C95.1 – 1991.
3. Juergen F. Kolb, Susumu Kono, and Karl H. Schoenbach, "Nanosecond Pulsed Electric Field Generators for the Study of Subcellular Effects," *Bioelectromagnetics J.* 27, 172-187 (2006).
4. Tammo Heeren, J. Thomas Camp, Juergen F. Kolb, Karl H. Schoenbach, Sunao Katsuki, and Hidenori Akiyama, "250 kV Subnanosecond Pulse Generator with Adjustable Pulsewidth," *IEEE Trans. Dielect. Electr. Insul.* 14, pp. 884-888 (2007).
5. Karl H. Schoenbach, Shu Xiao, Ravindra P. Joshi, James T. Camp, Tammo Heeren, Juergen F. Kolb, and Stephen J. Beebe, "The Effect of Intense Subnanosecond Electrical Pulses on Biological Cells," *IEEE Trans. Plasma Science* 36, pp. 414-424, 2008.
6. J. Thomas Camp, Shu Xiao, Stephen Beebe, Peter F. Blackmore\*, and Karl H. Schoenbach, "Bioelectric Studies with Subnanosecond Pulsed Electric Fields," *Digest of Technical Papers, 2009 IEEE Pulsed Power Conference*, Washington, DC, June 2009, p. 876.
7. "Electromagnetic Compatibility (EMC) Course Notes", Module 3, Michigan State University, <http://www.egr.msu.edu/em/research/goali/notes/>
8. C.E. Baum, "Electrode Design for Concentration of Electric Field at Skin Cancer," *Bioelectric Note 1*, April 2008.
9. C.E. Baum, "Impedances and field Distributions for Symmetrical Two Wire and Four Wire Transmission Line simulators," *Sensor and Simulation Note 27*, October 1966.
10. C.E. Baum, "Focal Waveform of a Prolate-spheroidal Impulse-radiating Antenna," *Radio Science*, Vol 42, RS6S27, 2007, 11pp.
11. S. Altunc, C.E. Baum, C.G. Christodoulou, E. Schamiloglu, "Focal Waveforms for Various Source Waveforms Driving a Prolate-spheroidal Impulse-radiating Antenna (IRA)," *Radio Science*, Vol. 43, RS4S13, 2008, 9 pp.
12. S. Altunc, C.E. Baum and C. Christodoulou, "Numerical Calculation for the Waveforms Near the Second Focus of a Prolate-spheroidal IRA," *EM Implosion Memo 7*, November 2006.
13. S. Altunc, C.E. Baum and C. Christodoulou, "Modelling a Lens with Dielectric Constant Inversely Proportional to Radius Squared," *EM Implosion Memo 21*, April 2008.
14. K.H. Schoenbach, C.E. Baum, R.P. Joshi, and S.J. Beebe, "A Scaling Law for Bioelectric Effects of Nanosecond Pulses," *Bioelectric Note 2*, June 2008.
15. Karl H. Schoenbach, Carl E. Baum, Ravindra P. Joshi, and Stephen J. Beebe, "A Scaling Law for Membrane Permeabilization with Nanopulses" special issue on "Bioelectrics" in the *IEEE Trans. Dielectrics and Electrical Insulation*, 16, 1224-1235 (2009).