Effects of laser irradiation on the central nervous system

II. The Intracranial Explosion

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One of the more interesting aspects of our study of the effects of laser radiation on intracranial structures has been the search for the mechanism of immediate death of guinea-pigs following passage of a single pulse train of laser energy through the intact skull. Laser light is a form of electromagnetic radiation but differs from other light sources in several important respects (Lengyel, 1962; Schawlow, 1963; Troup, 1963; Brotherton, 1964; Heavens, 1964). Laser light exhibits strong temporal coherence: the energy is emitted in a very narrow frequency bandwidth so that the wavelength does not vary. Because the electromagnetic waves are nearly all in phase from one point in time to the next (constant frequency), the light is extremely monochromatic, yet intense. This light also exhibits spatial coherence: the electromagnetic waves are almost all in phase laterally from one point in space to the next. This coherent beam can thus be brought to an extremely small focus by a lens system affecting very high energy concentration. Finally, by using a pulsed system rather than a continuous emission (continuous wave) system, it is possible to deliver the energy in an extremely short period of time, thereby increasing the power by several orders of magnitude. One of the effects of this latter phenomenon is that the heat generated at the living tissue target is absorbed faster than it can be conducted away.

Fine, Klein, Nowak, Scott, Laor, Simpson, Crissey, Donoghue, and Derr (1965) and Earle, Carpenter, Roessmann, Ross, Hayes, and Zeitler (1965) demonstrated that pulsed laser irradiation of sufficient energy-density was lethal to these animals when the intact cranium was radiated. At the Armed Forces Institute of Pathology we set out to find the mechanism of death in these animals (Fox, Hayes, Stein, and Green, 1966a; Fox, Stein, and Hayes, 1966b; Hayes, Fox, and Stein, 1967; Fox, Hayes, Stein, Green, and Paananen, 1967). The results of

these studies indicated that, when a single pulse train containing 12 to 24 cal* of 694 nm† wavelength laser energy and lasting 1.5 to 2.5 msec intercepts the exposed intact skull of a guinea-pig, extremely high intracranial pressures exceeding 10 atmospheres for 1 msec are attained. This occurs even though only 10% of the energy actually reaches the brain through the skull. This leads to brain-stem herniation and immediate, permanent respiratory arrest. The heart continues beating for about 10 minutes until anoxic arrest occurs. When the exposed brain was radiated the animal did not immediately die since, although 10 times as much energy struck the brain, the intracranial cavity was not closed. The rapidly expanding vapours were dissipated into the open air. We elected to study further the intracranial pressure phenomenon using high speed cinematography.

METHOD

Fifty white guinea-pigs were utilized during this study. The results have been reported (Fox *et al.*, 1966a; Fox *et al.*, 1966b; Hayes *et al.*, 1967; Fox *et al.*, 1967), except for the following photographic evidence of an intracranial explosion occurring during laser-skull interaction. Details of the laboratory set-up and technique used at the Armed Forces Institute of Pathology are given elsewhere (Hayes *et al.*, 1967; Fox *et al.*, 1967). Figure 1 is an illustration of some of the laser equipment (Maser Optics Model 3100 Laser Unit) which utilizes a ruby crystal cooled with liquid nitrogen. The guinea-pigs were anaesthetized with urethane (250 mg/ml. solution; 2 mg/g body weight) administered intraperitoneally. The high speed (3200 f.p.s.) cinematography was carried out with a Kodak Instex camera and Tri-X film with a 6 mm thick BG-18 copper sulphate filter to prevent over-exposure of the film. Fifteen minutes before laser

*24 small calories (cal) equals 100 joules (J) of energy. Energy-density usually is given in J/cm². One J/sec equals one watt (W) of power. Power-density is given in W/cm².

†The use of the nanometer (10⁻⁹ meter) or nm measurement is becoming standardized. 1 nm = 1 mμ = 10 Å.

FIG. 1. Photograph of experimental set-up. From left to right: target supported by ring stand and jack; focused laser beam (red, 694 nm) striking frontal region of guinea-pig (arrow); f-1 lens focusing laser beam (double crossed arrow); glass beam splitter (two short arrows) diverting a known small fraction of the light 90° away into a ballistic thermopile (single crossed arrow); Maser Optics 3100 Laser Head Containing the xenon flash lamps surrounding the ruby crystal emitting laser energy in the direction of the large arrow; frosted coils on top bringing liquid nitrogen around the optical cavity; a lamp projecting white light (white arrow) down the optical axis through the ruby rod and lens system for preliminary focusing. In the foreground is another ballistic thermopile which can be substituted for the target. The high voltage power supply, control panel, and several measuring instruments are located around this set up. AFIP Neg. 65-5728-1.

FIG. 2. Real time-dimensional tracing of a reflected fraction of a 40 J laser pulse train. Detected by an EG & G SD-100 photodiode and displayed on a type 555 Tetrox oscilloscope. Horizontal time base: 200 μ sec/cm. Vertical scale: intensity in arbitrary units. The baseline is elevated by pumping light from the xenon flashlamp in the laser head. Note that the 1.7 msec 'pulse' of laser radiation is actually a pulse train made of many short spikes of pulses, each of higher power (energy/sec) than the average power of the entire pulse train. AFIP Neg. 65-5728-2.

irradiation of the exposed intact guinea-pig skull the animal received 5% fluorescein intraperitoneally. (1 ml./kg body weight). Fifteen minutes after irradiation the animal was perfused with buffered formalin solution, and the brain was photographed under ultraviolet light (Hayes *et al.*, 1967).

RESULTS

A typical oscilloscope tracing of the relative laser energy distribution in real time is seen in Fig. 2. Notice that many small pulses make up the single millisecond pulse train. When such a single 24 cal pulse train of 694 nm wavelength laser energy is focused down to 1 mm² on the intact exposed skull of the guinea-pig and delivered in 2.5 msec, an explosive reaction takes place on the skull surface (Fig. 3). At focus the skull is superheated (approaching an estimated 6000° K) causing burning and vaporization of the skull to cause a 1 mm diameter perforation. The high-speed cinematography reveals what cannot be seen by visual observation. A plume of vapour and particles is blown off the skull causing the head to recoil a few centimetres in the opposite direction. The plume is illuminated by the laser beam and by self incandescence. Profile cinematography previously demonstrated submento-vertical expansion of the entire skull for a 1 msec interval (Fox *et al.*, 1967). Severe damage frequently occurred to the eyes, for on several occasions one or both eyes ruptured partially out of their sockets during remotely located laser impact to the skull.

When the brain under the laser focus is examined grossly, only some local subarachnoid bleeding and local intracerebral petechiae are seen (Hayes *et al.*, 1967; Fox *et al.*, 1967). Examination of the same area for evidence of blood-brain barrier injury using fluorescein tracer and ultraviolet light reveals only local injury insufficient to explain the death of the animal (Fig. 4). However when the brain is turned over and its base examined under ultraviolet light, brilliant fluorescence of the brain-stem (especially the pons) and often the base of the frontal and temporal lobes is seen (Fig. 5). Since the laser energy cannot transmit through the brain, some other explanation is needed. The same phenomenon is seen regardless of where the skull is intercepted by the laser beam, indicating this is not a contra-coup lesion.

In order to see what was happening to the brain-stem when the surface of the intact frontal bone was radiated, a guinea-pig was killed with an overdose of pentobarbital and then decapitated. The scalp was removed, and the base of the skull and foramen magnum were photographed at 3200 f.p.s. (0.313 msec between the onset of each frame) during

laser-skull interaction. Figure 6 shows the result of explosive conversion of less than a milligram of frontal brain tissue into a rapidly expanding vapour state. The entire contents of the posterior fossa shoot out of a foramen magnum at about 33 miles/hr. Finally the cerebral hemispheres begin to exit likewise, but then the tremendous overpressures rapidly recede and suck the cerebrum back into the cranium. The cerebellum and brain-stem meanwhile have struck the ceiling of the laboratory.

DISCUSSION

The actual pressures generated during the foregoing laser-skull interaction have not yet been measured by us. Development of a rugged pressure transducer of small size, sufficient frequency response, and adequate pressure range is difficult but is in progress. Meanwhile, the pressures involved can be estimated from the cinema frames and the impulse-momentum formula:

$$Ft = mv,$$

where F is the unknown force, t is the impulse time, m is the mass of brain ejected through the foramen magnum, and v is the velocity achieved by this mass. By knowing the interval between each cinema frame (0.313×10^{-3} sec) and by measuring the distance travelled between frames by the leading edge of the brain (0.46 cm), it is possible to estimate the velocity (v) to be 1470 cm/sec (or 33 miles/hr). The impulse time (t) must be 0.313 msec or less, since this velocity is achieved within the duration of one framing interval. The total mass of brain ejected was about 1 g, but it took four time frames to eject this, so the mass (m) is 0.25 g. Therefore $F = 1.2 \times 10^6$ dynes or 1200 g-wt. or 2.64 lb.-wt. If the area of the foramen magnum is about 0.13 cm² or 0.02 in.², the intracranial pressure is 130 lb./in.² or 9 atmospheres. This preliminary estimation does not take friction into account; the actual pressure most likely is over 20 atmospheres for 1 msec.

Laser damage is produced when energy is absorbed in the tissue faster than it can be dissipated. While the total energy absorbed by the brain may seem insignificant (2.4 cal), the lethal damage is due to a very small amount of tissue (less than 1 mg) absorbing energy so rapidly (2.5 msec) that tissue is vaporized before the heat can be conducted away. Ten joules of energy $\times 1/10^{-2}$ focal area $\times 1/(2.5 \times 10^{-3}$ sec) gives a power-density of 400,000 W/cm² at the brain surface, an indication of the very rapid transfer of energy into a very small area. Calculations based upon the results of these studies indicated that the outer 100 μ guinea-pig brain under the point of laser skull interaction absorbed about 625 cal/g—

FIG. 3a

FIG. 3. Cinematographic sequence (3200 f.p.s.) of laser-skull interaction. A dose of 90 J of energy is delivered in 2.5 msec and brought to a primary focus of 1 mm diameter on the intact 0.5 mm thick parietal bone of the guinea-pig. Four frames are excerpted from the 13 frame series of primary laser-skull interaction. AFIP Neg. 66-8123-1.

(a) Diagram of pre-radiation frame (b). Note sagittal suture (1) and coronal suture (2).

(b) Animal supported on its left side facing the camera before radiation. Skull is exposed through midline incision and its superior surface faces the focusing lens on the left. Arrow indicates trajectory of laser beam.

(c) Laser light begins to illuminate right parietal bone near sagittal-coronal suture conjunction.

(d) Plume exploding off the skull during laser-skull interaction. Arrow indicates direction plume is going.

(e) Post-radiation frame showing 1 mm perforation in skull surrounded by halo of still self-incandescent bone (arrows). Although the laser beam lasted 2.5 msec, the incandescence lasted about 3.5 msec.

FIG. 3b

FIG. 3c

FIG. 3d

FIG. 3e

FIG. 4. Fluorescence of zone of laser injury to cerebral hemisphere of guinea-pig brain cut in coronal section. The remainder of the cerebral hemisphere is not seen, since it was photographed under ultraviolet light following intraperitoneal administration of fluorescein. AFIP Neg. 65-5474-6.

enough energy concentrated in the tissue to vaporize tissue water and create destructive overpressures (Fox *et al.*, 1967).

It must not be forgotten that visible light is absorbed exponentially according to $E(l-e^{-\alpha x})$ where E = energy, e = base of natural logarithm, α = absorption coefficient (about 5 cm^{-1} for 694 nm) (wavelength in brain and skull tissue), and x = distance in cm travelled by the light. Hence any attempt to destroy selectively any tissue at a deeply placed focal point will not be successful. Most of the energy will be used up in destruction of the more superficial tissues first.

Transmission of a lethal amount of pulsed laser energy through the human scalp and skull would require impractical and phenomenally high energy fluxes and power-densities because of the high absorption coefficient (α) involved. Nevertheless, electro-optic advances in laser research are occurring rapidly, and tomorrow may see availability of very high power, high energy laser instruments. We know that, although the brain weight of a dog is about 20-fold that of the guinea-pig brain, less than a 10-fold increase of laser energy entering the intracranial cavity under similar conditions of power-

density is required to be immediately lethal to the dog (Fox *et al.*, 1967), and these findings can be extrapolated to the human. In other words, a large amount of delivered energy is needed to transmit through the scalp and skull the very small amount of lethal energy absorbed by the brain.

One can increase the total energy delivered by using a continuous wave (CW) laser system, which cannot match the billion watts of power delivered by the pulsed system but which can deliver at least up to 1000 W of power continuously. Previous investigations with the lower powered CW laser beam indicate that 4 W argon gas laser power at 400 W/cm^2 power-density will effectively cut through tissue slowly, and a 100 W of $\text{N}_2\text{-CO}_2$ gas laser power at 1000 W/cm^2 will burn rapidly through tissue (Fox *et al.*, 1967). Whether such CW laser radiation can cause explosive intracranial pressure changes requires study.

FIG. 5. Base of guinea-pig brain and brain-stem photographed under ultraviolet light only. Note brilliant fluorescence of (from below upwards) the medulla, pons, cerebral peduncles (arrows), hypothalamus, and part of base of temporal lobe. Non-fluorescent part of brain is not recorded on the film. Rostral portion of brain is above. AFIP Neg. 65-5474-7.

FIG. 6a

FIG. 6. While the 90 J laser beam strikes the frontal portion of the intact skull (see Fig. 3), the following sequence of events is occurring at the foramen magnum. Four frames are abstracted from the entire series. AFIP Neg. 66-8123-2.

(a) Diagram of pre-radiation frame (b). Base of head severed from body and directed upwards. Note brain-stem protruding at foramen magnum.

(b) Decapitated skull has right ear facing camera and nose is downwards out of sight. Two large arrows point to foramen magnum, the lower arrow extending from the right ear. The smaller horizontal arrow points to the superior surface of the skull and parallels the direction the laser beam will take.

(c) At 1.25 msec after onset of laser-skull interaction the brain-stem and cerebellum have shot out the foramen magnum in the direction represented by the arrow. The lower right-hand corner of the photograph is over-exposed by the unseen laser beam.

(d) Picture at 0.616 msec later.

(e) Picture at 5.6 msec after onset of laser-skull interaction. Contents of cerebellum are out of sight. Cerebral hemispheres (arrows) are seen protruding from foramen magnum.

FIG. 6c

FIG. 6d

FIG. 6b

FIG. 6e

We feel that the cause of death in the animals investigated is due to extremely rapid conversion of a small bit of brain tissue into a gaseous state—an intracranial explosion. The rapid expulsion of the guinea-pig brain through the foramen magnum (Fig. 6) is further evidence for this theory. The contributing effects of shock waves generated by laser-skull interaction cannot be clarified until adequate pressure transducers can be applied.

SUMMARY

This study of laser radiation was carried out to provide further evidence that very little total energy is required to be immediately lethal to the guinea-pig when the brain absorbs this energy faster than it can be conducted away. The laser beam must be focused to a high energy-density, and the brain tissue must absorb the energy inside the closed intracranial cavity. High speed cinematography shows clear evidence that we are dealing with intracranial pressures of hitherto unrecorded magnitude and rapidity.

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The 'Principles of Laboratory Animal Care' as promulgated by the National Society for Medical Research were observed during this study.

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