Shedding Light on Cancer

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An exciting application for lasers in medicine is photodynamic therapy (PDT). PDT is a unique form of cancer therapy capitalizing on a photochemical reaction. Modern use of PDT is limited to the past 40 years, however ancient physicians used similar methods to treat diseases as early as 1200 BC.

PDT involves giving a light-activated drug, called a photosensitizer, to the patient and then irradiating the tumor with visible light. Because of the mechanism of action, PDT is a highly selective form of cancer therapy, especially when compared to ionizing radiation therapy or systemic chemotherapy. Neither the visible light nor photosensitizer causes any harmful tissue effects. Tissue damage only occurs with the presence of photosensitizer, light of the appropriate wavelength, and molecular oxygen simultaneously. The wavelength of light used for treatment will correspond to the peak absorption wavelength of the photosensitizer. The photosensitizer absorbs a photon and is then activated to an excited singlet or triplet state. The activated photosensitizer can then react with oxygen or any nearby molecule to cause oxidative cellular damage.

Photochemical reactions can directly kill cancer cells, but the majority of tumor destruction comes from PDT-induced vascular collapse, thrombosis, and subsequent ischemia. PDT also causes an influx of inflammatory cells to the treatment site. Regression of PDT-treated tumors is rapid, and can occur within days of treatment.

Historically, PDT has been done with laser light sources. The Argon-pumped tunable dye laser is widely used in the research setting because it is capable of producing wavelengths of light corresponding to all currently available photosensitizers. However, this laser system is not clinically useful due to its size, expense, and need for specialized electrical and plumbing connections. Portable diode lasers are readily available for PDT. However, unlike the tunable dye lasers, a diode laser produces a single wavelength of light, meaning a diode laser is only useful with one photosensitizer. A major limitation to widespread application of PDT in man and animals has been the expense of lasers. As a result, there are non-laser light sources currently being developed for PDT applications.

Most of the photosensitizers being studied for PDT are activated by visible red light (630 – 675 nm), which is readily transmitted through tissues. Visible red light may travel up to 0.5 cm in tumor tissue, making PDT well suited for superficial tumors. One advantage of laser light is that it can be delivered through small diameter (ca. 400 micron) optical fibers, permitting the treatment of tumors in viscera using flexible endoscopy. Likewise, these small fibers can be inserted directly into tumors for interstitial PDT. For surface irradiation of skin tumors, optical fibers are most often fitted with a microlens to ensure uniform energy distribution. Optical fibers terminating in cylindrical diffusers are used for interstitial or intraluminal irradiation. Because of the small size of these optical fibers, virtually any site in the body is accessible for PDT. Laser fibers terminated in a microlens

produce a circular spot whereas the cylindrical diffusers produce a column of light.

The amount of light required for PDT is much less than that used for surgical laser applications and does not heat the tissus. The two important parameters for PDT light dosimetry include 1) energy density, or light dose, which refers to the amount of light (Joules) delivered to a given area and is expressed as J/cm^2, and 2) power density, or dose rate, which refers to the rate of light delivery (Watts) to a given area and is expressed as W/cm^2. Both energy density and power density influence the efficacy of PDT. Increasing energy density improves PDT efficacy, whereas decreasing power density improves PDT efficacy. However, increasing energy density or decreasing power density increases the length of a PDT treatment, which becomes an important consideration for general anesthesia time.

Photosensitizers are generally given to the patient by intravenous injection, however some photosensitizers, such as 5-aminolaevulinic acid, can be given orally, applied topically, or instilled intravesicularly. Most photosensitizers preferentially accumulate in neoplastic tissue over time due to several mechanisms related to characteristics of the tumor and drug itself. The delay between photosensitizer administration and light treatment allows for maximal tumor concentration and minimal normal tissue concentration, thereby increasing the tumor selectivity of PDT. This interval can range from hours to days depending on the photosensitizer.

There are many photosensitizers that have been evaluated for use in veterinary medicine. These include (with activating wavelength):

Aluminum and zinc phthalocyanine (675 nm)
Pheophorbide-a-hexyl ether (665 nm)
Sn-ethyl etiopurpurin (660 nm)
Meta-tehtrahydroxyphenylchlorin (652 nm)
5-Aminolaevulinic acid (635 nm)
Hematoporphyrin derivative (630 nm)

At present information about the pharmacokinetics in dogs and cats of most photosensitizers is lacking, which is a major obstacle to developing optimized PDT protocols. Although most photosensitizers appear safe for use in dogs, adverse liver effects in cats have been reported with 5-aminolaevulinic acid and aluminum phthalocyanine.

PDT has been most commonly used to treat squamous cell carcinoma in veterinary medicine, although other tumor types have been treated in smaller numbers. Response rates have been reported as high as 90%, depending on tumor size and stage, with long-term survival described in some animals. Although thousands of people have been treated with PDT worldwide, PDT is still considered an investigational therapy in veterinary medicine.