Light-Based Ablative Therapies (LBAT) – Lighting up the dark corners of malignant micro-environment

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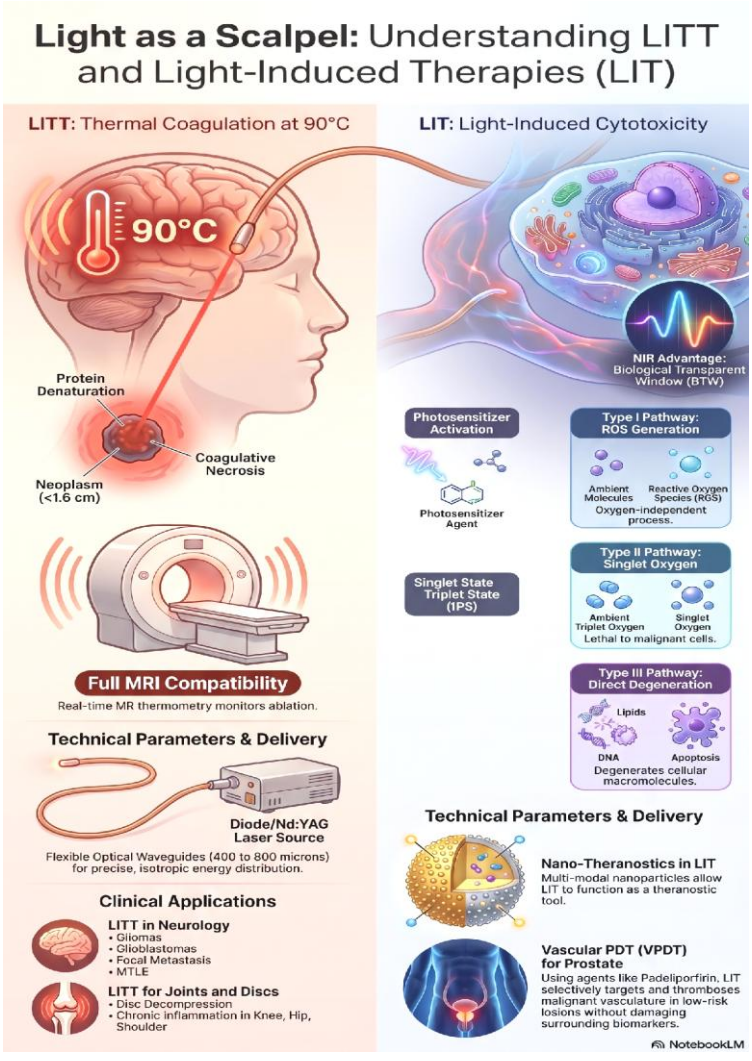
***Abstract*—Laser Interstitial Thermal Therapy (LITT) and Light-Induced Therapies (LIT)—comprising Photodynamic Therapy (PDT) and Photothermal Therapy (PTT)—represent a paradigm shift in minimally invasive interventional oncology and neurology. LITT utilizes MRI-compatible laser probes to deliver precise thermal energy, primarily for deep-seated intracranial lesions and musculoskeletal pathologies. In contrast, LIT leverages the interaction between specific wavelengths of light and photosensitizing agents to induce localized cytotoxicity via reactive oxygen species (ROS) or hyperthermia. This article explores the physics of laser-tissue interaction, chemical pathways of phototoxicity, current clinical applications in neuro-oncology and joint therapy, and the future role of nanoparticle-mediated theranostics.**



I. Physics and Mechanisms of Action

1. Thermal Mechanism (LITT)

LITT is characterized by its **complete MRI compatibility**, making it the gold standard for real-time monitoring of thermal ablation in the brain.

- **Energy Delivery:** A coherent, monoenergetic beam is delivered through waveguides (optical fibers). Probes are often actively cooled with water or CO_2 to protect the fiber and allow for higher energy deposition.
- **Therapeutic Parameters:** It maintains a conservative tissue temperature of approximately **90°C**. The ablation zone is calculated using the **Arrhenius model** or **Cumulative Equivalent Minutes (CEM 43)**.
- **Sizing:** Currently optimized for small neoplasms, typically those **<1.6 cm in diameter**.

2. Chemical and Photo-activation Mechanisms (LIT: PDT & PTT, Figure 1)

LIT utilizes near-infrared (NIR) light, which can penetrate tissue through the **"biological transparent window" (BTW)** to activate external agents.

Step-wise activity:

1. **Activation:** NIR Light Photon hits a **Photosensitizer** (e.g., ICG derivatives, 5-ALA).
2. **Excitation:** Photosensitizer moves to an **Excited Singlet State**, then via **Intersystem Crossing** to a **Triplet State (tPS)**.
3. **Cytotoxic Pathways:**
   - **Type I (Oxygen Independent):** tPS reacts with molecules to form free radicals, which then produce **ROS** (Reactive Oxygen Species) upon contact with water/oxygen.
   - **Type II (Oxygen Dependent):** tPS reacts with triplet oxygen to form **Singlet Oxygen**, a highly volatile and lethal species.
   - **Type III:** tPS directly degenerates macromolecules without intermediate species.
   - **PTT Pathway:** tPS undergoes non-radiative relaxation, converting light energy into **localized heat (>47°C)**.

Clinical Applications (Table 1)

Field	Application	Details
Neurology (LITT)	Gliomas, Glioblastomas, Epilepsy (MTLE)	Uses stereotactic robots or frameless guides (e.g., **Visualase, Monteris**) for burr-hole access.
Neurology (LITT)	Radiation Necrosis, Hamartomas	Effective for deep-seated lesions where surgery is high-risk.
Musculoskeletal	Joint Cavities & Discs	Used for **disc decompression**, spinal stenosis, and anti-inflammatory therapy in large joints (knee, hip, frozen shoulder).
Urology (VPDT)	Prostate Cancer	**Vascular PDT (VPDT)** using **Padeliporfirin** causes selective vessel thrombosis in low-risk prostate lesions.
General Oncology	Small Neoplasms	Applicable where precise margins are required near metallic implants.

II. Future Directions

- **Nanoparticle Enhancement:** Using gold (Au), silver (Ag), or copper (Cu) nanoparticles for favorable **plasmonic properties** in PTT.
- **Theranostics:** Utilizing nanoparticles as **multi-modal carriers** for both diagnostic imaging and targeted medication release (e.g., UTMD—Ultrasound Targeted Microbubble Dispersion).
- **"Self-Immolating" Molecules:** Light-sensitive molecules that act as scaffolds, disintegrating upon laser application to release active chemotherapy directly into a tumor.
- **Photoimmunotherapy:** Combining PTT with **monoclonal antibodies** (e.g., anti-PSMA-IR700) to target specific malignant biomarkers.

III. Conclusion

Laser-based therapies offer unparalleled precision due to their MRI compatibility and ability to target malignant cells through molecular pathways rather than just heat. While LITT is the primary thermal choice for neurological and spinal applications, the evolution of LIT and nanoparticle-mediated theranostics promises a future of highly selective, biomarker-independent cancer treatment.

Figures

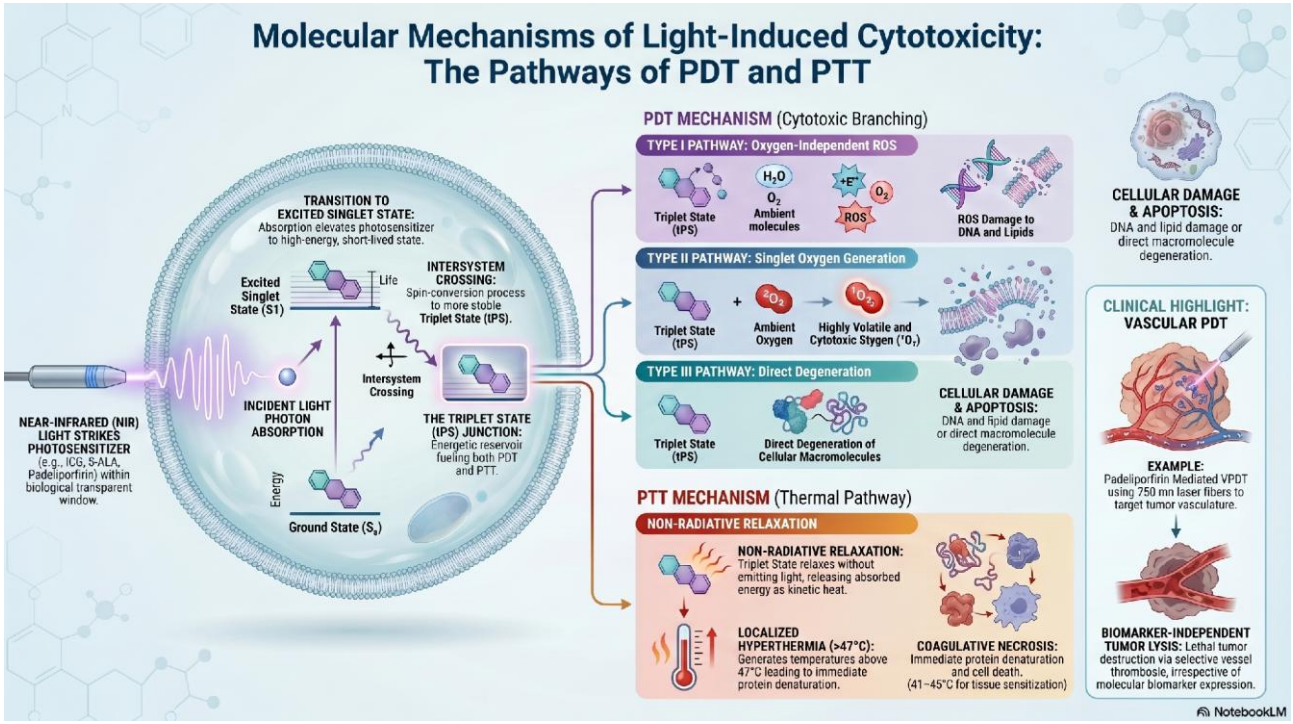


Figure 1: Chemical mechanisms in light based ablations

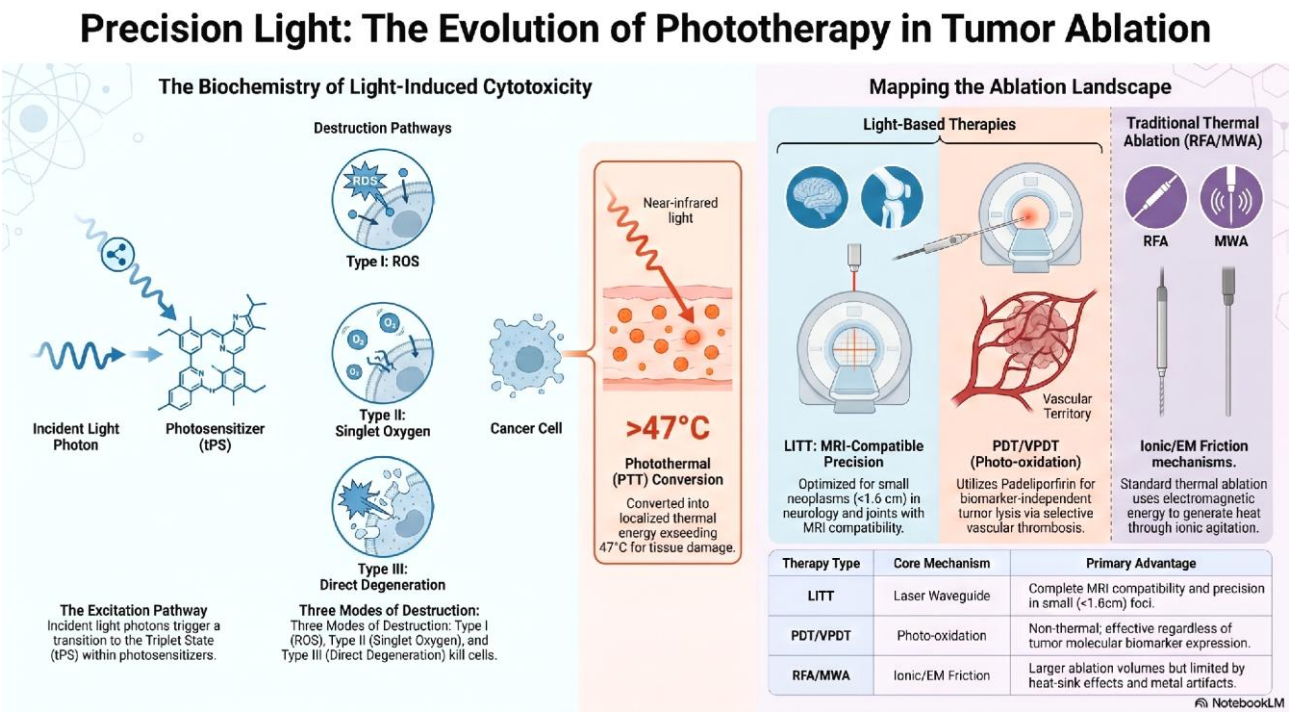


Figure 2: Phototherapy's role in the larger ablation milieu

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Intellectual inputs – Dr. Reetoja Das

Logistical support – Mrs. Sima Patra (Bhandari)

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