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MINI REVIEW

Advancing Thermal Cancer Therapies: The Role of Mathematical Oncology in Precision Medicine

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Abstract

Mathematical oncology is pivotal in advancing thermal cancer therapies, such as radiofrequency ablation, microwave ablation, and cryoablation, which provide minimally invasive alternatives for patients ineligible for surgical intervention. This review underscores the role of mathematical modeling in optimizing treatment strategies through precise planning, real-time monitoring, and adaptive adjustments. By integrating tumor characteristics, heat distribution, and treatment responses, these models may enhance the efficacy of thermal therapies. Challenges in model validation, clinical integration, and scalability are discussed, alongside future directions that emphasize the development of multi-scale, adaptive models incorporating immunological and pharmacological interactions. Ultimately, mathematical oncology bridges theoretical insights with clinical applications, significantly advancing precision medicine in thermal cancer treatment.(**International Journal of Biomedicine. 2025;15(3):457-460.**)

Keywords: thermal therapy • ablation • tumor • mathematical oncology

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Introduction

Cancer remains one of the leading causes of mortality worldwide, with an estimated 29.9 million new cases projected by 2040.[1,2] Given cancer's status as a global health problem, ongoing research is essential to discover new treatment options and improve existing ones to increase survival rates.[3,4] Among the available cancer treatments, thermal therapy, which utilizes heat to destroy cancer cells, is recognized as a flexible, cost-effective, and minimally invasive option, particularly for patients who cannot undergo surgery.[5,6] This has led to a growing emphasis on personalized oncology—therapeutic strategies tailored to individual tumor biology, patient-specific physiology, and real-time treatment responses.

Thermal therapy offers a minimally invasive alternative for localized tumor destruction, particularly beneficial for patients who are not candidates for conventional surgery.[7] Techniques such as radiofrequency ablation (RFA), microwave ablation (MWA), and cryoablation enable targeted tumor destruction while preserving surrounding healthy tissue.[8] Moreover, emerging evidence supports the synergistic effects of combining thermal therapy with other modalities, including chemotherapy, radiation therapy, and immunotherapy, to enhance overall therapeutic efficacy (Figure 1).[9]

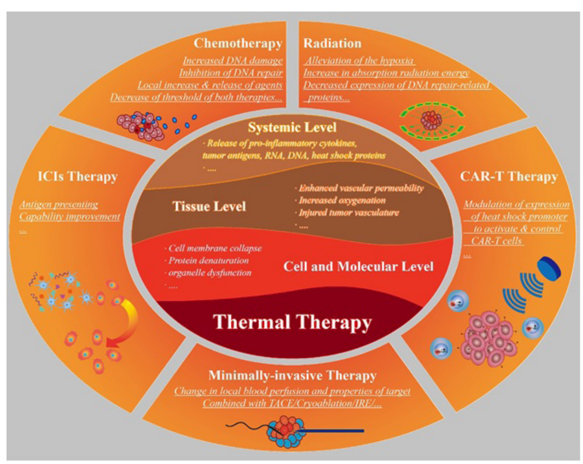

Figure 1. *Schematic of synergetic thermal therapies, illustrating effects at the cellular, tissue, and systemic levels. This synergy enhances chemotherapy, radiation, immunotherapy, and minimally invasive treatments.*

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This review examines the current state of mathematical oncology in thermal cancer therapy, highlighting its capabilities, limitations, and contributions to advancing patient-specific treatment planning and predictive therapeutic strategies. By connecting theoretical modeling with clinical applications, mathematical oncology has significant potential to enhance the precision, safety, and efficacy of thermal therapies. Understanding these modeling frameworks is essential for developing robust, evidence-based treatment protocols that fully leverage the capabilities of thermal therapy in modern oncology practice.

Mechanisms of Thermal Therapy

The goal of thermal therapy is to alter tissue temperature in a targeted region over time to induce a desired biological response.[10] There are multiple forms of thermal therapy. Based on the operative temperature, thermal therapy could be divided into three categories: thermal ablation (>55 °C), hyperthermia (>39–45 °C), and cryoablation (<−40 °C). Radiofrequency ablation (RFA), Microwave ablation (MWA), and Cryoablation (CA) are the main ablative techniques (Figure 2). All of them are mostly overlapping in terms of cancer-specific free survival and outcomes.

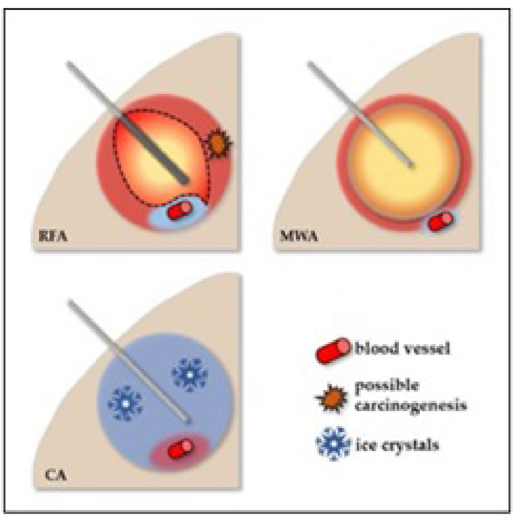

Figure 2. *Schematic overview of the thermal ablative therapies and their effects. RFA, radiofrequency ablation; MWA, microwave ablation; CA, cryoablation. The applicator was positioned in the tumor under guidance.*

RFA utilizes high-frequency alternating current (200-1,200 kHz) delivered through insulated needle electrodes, either single or multiple (stereotactic RFA), to generate localized heat in tumors.[11] This heat, reaching temperatures between 50°C and 105°C, induces ion oscillation in the extracellular fluid, resulting in hyperthermic damage. The process leads to cell membrane dysfunction and protein denaturation, ultimately causing acute coagulative necrosis and cell death.

MWA is an effective thermal ablation method that serves as an alternative to RFA.[12] MWA utilizes antenna probes and frequencies between 900 and 2,450 MHz to heat tumors. The electromagnetic interaction between microwaves and biological tissues causes polar water molecules to oscillate, resulting in localized temperature increases. MWA can achieve hyperthermic temperatures up to 150°C, leading to tumor ablation through coagulative necrosis.

Cryoablation is a traditional ablative technique that employs compressed gases like carbon dioxide (CO_2), argon (Ar), helium (He), or nitrous oxide (N_2O) through metal probes or cryoneedles to freeze tumor tissues.[13] Achieving temperatures of -10°C or lower is essential for inducing cryonecrosis. This process causes cell injury and death through several mechanisms, including the formation of intracellular ice crystals, thrombus formation leading to ischemia, desiccation, and apoptosis. The duration of freeze-thaw cycles is tailored based on the type of tumor, whether in the lungs, kidneys, liver, bones, or cervix, to optimize treatment efficacy. Regardless of the treatment modality, these therapies are designed to deliver thermal therapy conformally to a target tissue volume while minimizing impact on surrounding tissues. A summary of the advantages, limitations, and performance of the thermal ablative therapies is provided in Table 1.[14]

Table 1.

Overview of the advantages, limitations, and 5-year survival rate of minimally invasive thermal ablative treatments (Microwave ablation, radiofrequency ablation, and cryoablation) for Hepatocellular carcinoma.[14]

Ablative methods	Advantages	Limitations	5-year survival rate
RFA	Better control for larger nodules	Not recommended for superficial lesions. Heat sink effect.	40-68%
MWA	Higher ablation volume. Minimal heat sink effect.	Ablation volume may be difficult toestimate. More complications in larger nodules.	50-60%
CA	Less painful. Area of CA visible on CT/MRI.	Cryoshock syndrome is a possible complication.	23-59%

Role of Mathematical Oncology in Thermal Therapy

Despite the unquestionable benefits of electromagnetic-based thermal therapies, the interaction between medical tools and tissue can lead to tissue damage, localized heating, and force feedback to the tools. According to data reported in 2024, the overall risk of complications from such thermal treatments is approximately 2-3%. One of the key challenges in safely and effectively implementing these therapies is the necessity of treatment optimization, often tailored to specific modalities to provide patient-specific care. Mathematical oncology provides essential tools for simulating, predicting, and optimizing thermal therapy outcomes. These models integrate physical laws, biological mechanisms, and patient-specific data to guide clinical decision-making[16] as depicted in Figure 3.

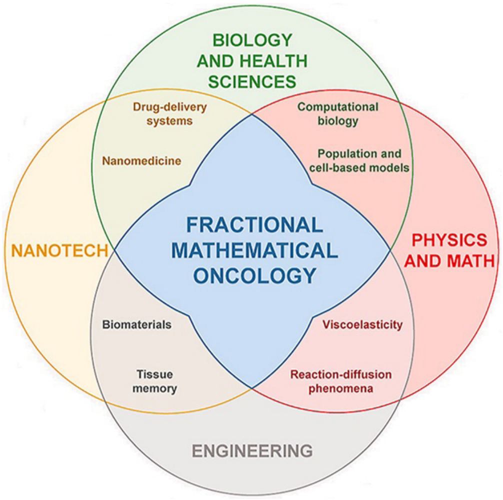

Figure 3. *Mathematical Oncology harnesses interdisciplinary insights, from biology to materials science, to develop comprehensive models that deepen our understanding of cancer dynamics and treatment strategies.*

Mathematical models, including differential equations and agent-based models, simulate tumor growth, angiogenesis (blood vessel formation), and metastasis (spread to other parts of the body).[17] These models can help predict how tumors will evolve over time and respond to different treatments. Mathematical models of thermal therapy procedures consist of three fundamental components. The first is the modeling of tissue and heat transport within tissues. The second pertains to the modeling of the electromagnetic field. The third component is associated with modeling the effects of heating on tumor cells.[18,19] Using MRI or CT imaging, models can be personalized to individual anatomy, enabling more accurate simulations of temperature profiles and tissue response. This is especially valuable for heterogeneous tumors or complex anatomical regions.

Although promising developments exist, several barriers hinder the widespread adoption of mathematical oncology in thermal therapy. First, high-quality patient-specific data is often limited, impacting model accuracy. Additionally, balancing accuracy with computational efficiency remains a challenge due to model complexity. Bridging the gap between theoretical models and clinical use requires further standardization for effective clinical validation. Finally, successful implementation demands close coordination among clinicians, mathematicians, engineers, and biologists to facilitate interdisciplinary collaboration.

Conclusions and Future Outlook

Mathematical oncology has become a cornerstone in advancing thermal cancer therapy. Through detailed modeling of heat transfer, tumor dynamics, and multimodal treatment effects, it supports the development of more precise, personalized, and effective treatment strategies. Current models already provide valuable insights into treatment planning and outcome prediction. However, future efforts should focus on integrating multi-scale, adaptive frameworks that incorporate real-time imaging, immune response modeling, and drug interaction simulations.

Emerging technologies such as machine learning, artificial intelligence, and high-resolution imaging will enhance predictive capabilities, enabling feedback-driven and adaptive therapies. Moreover, the synergy between thermal therapy and immunotherapy presents a promising frontier, where mathematical models could guide immune activation post-ablation.

To fully realize the potential of mathematical oncology in thermal therapy, continued investment in interdisciplinary research, computational infrastructure, and clinical validation is essential. As the field evolves, it holds the promise of transforming cancer care through precision-driven, patient-centered treatment paradigms.

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Conflicts of Interest

The authors declare no conflict of interest.

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