High Intensity Focused Ultrasound: Applications for Immunomodulation in Oncologic Treatment

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Introduction

High-Intensity focused ultrasound (HIFU) is revolutionary in non-invasive tumor ablation with significant immunomodulation.

This exhibit explores how HIFU influences tumor immunogenicity and evaluates its potential to enhance antitumor immune responses, particularly in combination with immunotherapies

Materials and

- Literature Review: Comprehensive literature review (2015-2024) using PubMed, Scopus, & Web of Science
- Search Terms: HIFU, Immunomodulation, immunogenic cell death, tumor immunity.
- Inclusion: Peer-reviewed articles on HIFU immunomodulatory effects, preclinical/clinical trials with immunotherapy combinations.
- Analysis: Categorized by HIFU mechanism (thermal vs. mechanical), cancer type, immune endpoints across 5 biomarker categories.

Results

Key Findings

- 47 studies analyzed (38 preclinical, 9 clinical trials)
- Multiple cancer types: prostate, breast, liver, neuroblastoma
- Mechanical HIFU superior to thermal for immune activation
- DAMP release triggers systemic response
- Enhanced dendritic cell activation in lymph nodes
- Significant survival improvements with combination therapy

Survival Rate Improvement:
0% -> 62.5% with combo therapy (P<0.0001)
Silverstrini, et al. Murine Neuroblastoma Model, Clin Cancer Res. 2020

Progression-Free Survival:
+138% improvement with combo therapy (4.60-10.95 months, p<0.001)
Overall Survival: **+84% improvement (10.67-19.6 months, p<0.05)**
Yang et al. Liver Metastases, PLoS ONE. 2024

IL-6 Expression: **+480% over baseline (p<0.05)**
Silvestrini at al. MR-guided in Murine Breast Cancer, 2021

TNF-a Expression: **+350% over baseline (P<0.05)**
Singh at al. Multiple. Sci Rep. 2019

CD8+ T-cell Infiltration: **+330% with combo therapy (P<0.01)**
van den Bijgaart, et al. Multiple. Front Immunol. 2022

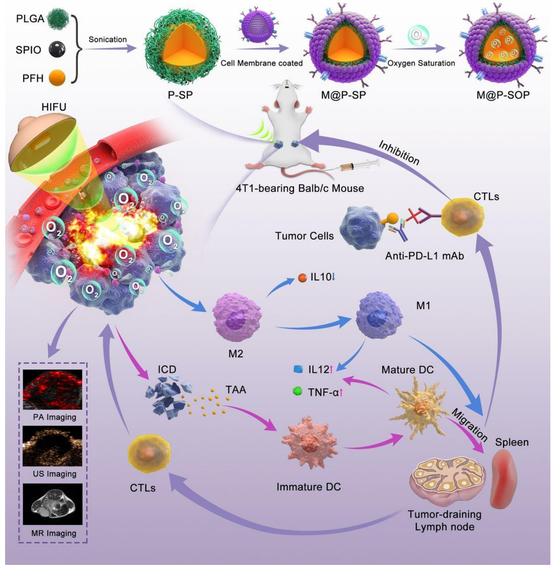

Fig. 2: HIFU-triggered tumor damage activates immune cells and enhances immuno-therapy. (van den Bijgaart, et al.)

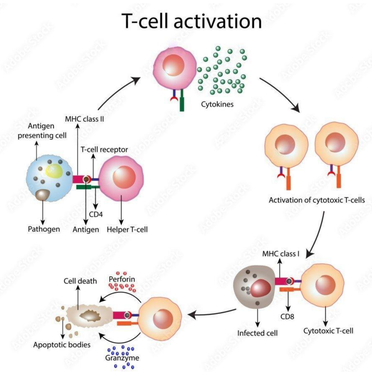

Fig. 3: Antigen presentation and T-cell response critical to HIFU-driven immunity. (Singh, et al.)

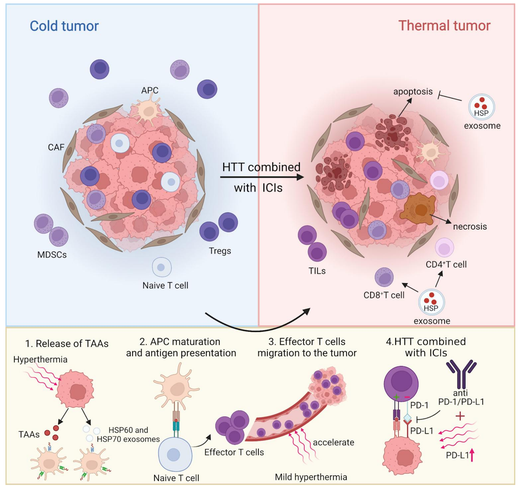

Fig. 1: HIFU-induced shift from immune-suppressive ("cold") to immune-active ("hot") tumors. (Silvestrini, et al., 2021)

Conclusion

HIFU represents a paradigm-shifting addition to immunotherapy, transforming "cold: tumors into "hot" immune-responsive environments.

Key findings indicate HIFU-induced immunogenetic cell death significantly amplifies checkpoint inhibitor efficacy through DAMP release, cytokine upregulation, and enhanced immune infiltration.

Mechanical HIFU shows greater immunomodulatory potential. Clinical validations reveals substantial survival benefits, positioning HIFU as a valuable precision tool in oncology with dual tumor debunking and immune activation capabilities.

Future research should prioritize clinical trials that integrate HIFU with immunotherapeutic regimens, aiming to optimize timing, dosage, and patient stratification for maximum benefit.

References

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