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ABSTRACTS

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GA101- Immunomodulatory Photoacoustic Nanoparticle-engineered Macrophages for Solid Cancer Immunotherapy and Longitudinal Monitoring

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Category: Oncology

Abstract Body:
Background: Reinforcing antitumor functions of macrophages, phagocytosis of cancer cells and secretion of inflammatory cytokines, can be a potent approach to treat solid tumors. Several strategies including CAR-macrophages and phagocytosis-enhanced macrophages (engineered via anti-CD47 antibody treatment) have been recently reported and have shown promise in preclinical models [1, 2]. However, these approaches lack mechanisms for monitoring transferred macrophages and assessing their therapeutic efficacy against tumors, limiting the ability to implement longitudinal therapeutic interventions throughout the treatment. Integrating imaging and contrast agents offers a possibility for real-time and non-invasive tracking of macrophages within the tumor microenvironment. Specifically, labeling macrophages with imaging contrast agents allows for longitudinal visualization of their migration, infiltration, and persistence in tumors, which could serve as an indicator of therapeutic response. Photoacoustic (PA) imaging is a technique that combines ultrasound and optical imaging by leveraging the light-to-sound conversion under laser irradiation of optical absorbers with high-intensity nanosecond laser pulses. PA imaging offers a powerful tool for real-time and noninvasive tracking of adoptively transferred cells. Here, we propose a macrophage engineering strategy for PA image-guided cancer immunotherapy. A nanoparticle formulation with both PA contrast and immunomodulatory effects is synthesized. Macrophages labeled with the formulated nanoparticles demonstrated strong antitumoral phenotypes and allowed longitudinal PA imaging. Our work provides perspectives on engineering macrophages for image-guided cancer immunotherapy.
Methods: Macrophages were derived from murine bone marrow cells. Bone marrow cells were extracted from the femur and the tibia from 5 - 8 weeks old mice. The cells were cultured with 20 ng/mL M-CSF for differentiation into macrophages. The hyperbranched gold nanoconstructs (HBGNCs) were synthesized via surface-blocker assisted seeded growth. Briefly, the surface of 35 nm-sized gold nanospheres was partially blocked during the seeded growth to yield the hyperbranched structure with a construct dimension of 100 nm.
For PA imaging, macrophages were labeled with HBGNCs. Afterwards, cells were washed with PBS and collected. The cell solution was embedded in gelatin phantom. The phantom was submerged in water and imaged under Vevo2100/LAZR imaging system.
The effect of particle labeling on key cellular functions, such as viability, migration, and antitumoral functions (CD80, CD87, MHCII, and CD206 expression), was investigated by confocal microscopy and flow cytometry.
Results: Photostable HBGNCs with high optical absorption efficiency, ~90% in the near-infrared I (NIR I) region, were synthesized. The enhanced optical absorption was attributed to the hyper-branched structure. Due to the enhanced optical responses at NIR I region, the HBGNCs produced robust photoacoustic (PA) responses at corresponding wavelengths, offering high sensitivity in PA imaging. When macrophages were labeled with HBGNCs, the size and the granularity of the cells increased as the particles were internalized. The labeling did not affect the viability of the cells. HBGNC-labeled macrophages embedded in tissue-mimicking phantoms yielded high PA signal.
The migration ability of the labeled macrophages was evaluated. Compared to IFNg-primed macrophages that are known to migrate at a high rate, macrophages labeled with either HBGNCs or HBGNC-Gs displayed a superior migration ability.
The phenotype of macrophages became more strongly anti-tumoral when labeled with IFNg-conjugated HBGNCs (HBGNC-Gs) compared to HBGNC and IFNg alone. This was supported by the increased expression of costimulatory receptors CD80 and CD86, MHCII, and the decreased expression of pro-tumoral marker CD206.
Conclusion: In the current study, a new strategy of macrophage engineering for cancer immunotherapy was introduced. Labeling macrophages with HBGNC-Gs have enabled PA imaging of macrophages and, at the same time, enhanced their migration ability and antitumoral phenotype. Results suggest that HBGNC labeling approach can provide insights into developing strategies for macrophage-based cancer immunotherapy.
Disclosures: The authors have no conflicts of interest to disclose.
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Poster Presentation

GA156- Development of Physics-informed nnU-Net for Glioblastoma Magnetic Resonance Image Segmentation

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Category: Computational & Data Science

Abstract Body:
Background: Glioblastoma (GBM) segmentation is particularly challenging due to the highly heterogeneous nature of the tumor. GBM exhibits significant variability in shape, size, and texture across different patients, making it difficult for models to generalize effectively [1, 2]. Moreover, the tumor consists of multiple subregions, including the necrotic core (NCR), enhancing tumor (ET), and edema (ED), each of which appears differently on MRI scans. These subregions do not always have clear boundaries, especially edema, which can infiltrate healthy tissue, making it difficult to distinguish tumor margins precisely. To improve segmentation accuracy, deep learning models like nnU-Net incorporate advanced pre-processing, data augmentation, and post-processing techniques. Standard nn-UNet architectures excel at learning statistical mappings from image intensities to labels, but they can struggle when the test data differ from the training distribution (for example, in different scanners, sequences, motion artifacts, or noise levels). Embedding physics into a nn-UNet could help address these shortcomings. To address this problem, we propose a physics-informed nn-UNET model based on the diffusion-reaction equation to guide the tumor segmentation process.
Methods: Dataset: The dataset used in this study (**https://wiki.cancerimagingarchive.net/display/Public/TCGA-GBM**) comprises MRI scans of Glioblastoma patients with T1, T1-GD (also called T1 post contrast, T1 contrast enhanced), T2, T2-FLAIR, which are critical for identifying tumor regions. **Data preprocessing**: nnU-Net automatically configured preprocessing pipelines, including intensity normalization, cropping, and resampling to isotropic resolution.
Model description: The nnU-Net framework was employed for its adaptability in medical image segmentation tasks. The 3D Full Resolution (3d_fullres) model was selected to handle volumetric MRI data with high spatial detail. The proposed model is nnUNet + Physics-informed boundary refinement using reaction-diffusion partial differential equations (PDEs). The model was trained using Google Colab, leveraging a T4 GPU for computational efficiency. The model was trained using the following hyperparameters: lnitial learning rate: 0.01, weight decay: 0.00003, epochs: 50, iterations per Epoch: 150, validation iterations per epoch: 50, foreground oversampling percentage: 33%. The physics-informed nnU-Net used a custom loss function that adds a diffusion-reaction term to the standard Dice and cross-entropy loss. The diffusion Coefficient (d), reaction coefficient (ρ) and PDE loss weight ($\lambda_p d_c$) were tuned as e tuned hyperparameters to provide better performance across metrics like Dice, recall, precision, HD95, and IoU as compared to the baseline model.
Results: From figures 1 and 2, the proposed model (physics-informed nnU-NET) produces a cleaner overall tumor shape when compared to the baseline nnU-NET. The model captured the tumor edges more accurately, which means there are fewer mis-classifications. The model does a better job outlining the active part of the tumor in the enhancing tumor region (label 3; yellow region). It avoids extending into nearby healthy tissue, resulting in sharper and more precise edges. The model also cleans up the boundaries of the tumor's core, labelled 1 (red region). There is less extra noise or stray pixels, making the core's shape align more closely with the ground truth. Table 1 show improved performance of the proposed model over the baseline nnU-NET model. As shown in table 2, a lower HD95 indicates that segmentations from the proposed model align more closely with the ground truth, significantly improving boundary accuracy (crucial in medical tasks like surgical planning). Both Dice and IoU were found to be higher with the proposed model, showing that it covered the tumor regions more completely and with fewer false predictions. While the proposed model showed slightly reduced precision (a small increase in false positives), it significantly boosts recall, meaning it correctly identifies more of the actual tumors and misses fewer tumor regions. In a medical context, higher recall is often more critical than a small dip in precision, because failing to detect tumor tissue can be riskier than a mild overestimation.
Conclusion: This study demonstrated that incorporating physics into deep learning specifically a diffusion-reaction loss constraint in nnU-Net - can meaningfully improve brain tumor segmentation as shown in the results. The model outperformed the baseline nnU-Net in terms of Dice score and Hausdorff Distance at the 95th percentile (HD95) across all major tumor sub-regions, especially in detecting the Tumor Core and Enhancing Tumor. The findings underscore the potential of physics-informed AI models in medical imaging and lay the foundation for future improvements combining domain knowledge with deep learning.

Disclosures: The authors have no conflicts of interest to disclose.
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Poster Presentation

GA160- Development and Implementation of Physics-Informed Segresnetunet for Brain Tumor Segmentation Using BRATS2020 Dataset

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Category: Computational & Data Science

Abstract Body:
Background: Accurate brain tumor segmentation is crucial for effective diagnosis and treatment planning in brain cancer cases. Traditional segmentation methods often fall short in capturing the complex nature of tumors. This study presents the Physics-InformedResNetUNet model, a deep learning framework that integrates a physics-informed layer simulating realistic tumor growth dynamics into U-Net's segmentation capabilities and ResNet's residual learning. The physics-informed component models thectumor growth using simplified diffusion equations, reflecting how tumors evolve spatially over time, thereby enhancing the network's understanding of tumor morphology.
Methods: Data Preprocessing: For model training, the Physics-Informed ResNetUNet model, preprocessing steps include: Normalization (scaling pixel values to 0–1 for consistency), resizing (standardizing image dimensions to match model input).
Data Augmentation: Techniques like random cropping, flipping, intensity normalization, and random intensity adjustments have been applied to increase data diversity and improve model robustness.
Model Architecture (Physics-Informed ResNetUNet): encoder (uses ResNet-based residual blocks for feature extraction), bottleneck (a deeper residual block captures complex features), decoder (3D transpose convolutions upsample and reconstructfeature maps), dropout (mitigates overfitting). The architecture is illustrated in figure 1.
Physics-Informed Layers: simulates tumor growth using an anisotropic diffusion equation, factoring in oxygen levels and necrosis.
Training Process: this includes batch processing, Dice loss calculation, and gradient updates. Physics-informed inputs simulate tumor growth to guide segmentation predictions.
Validation: Evaluated post-epoch with Dice scores for different tumor regions (core, whole tumor, enhancing tumor), and the best model was saved based on their performance. Key metrics tracked were learning rate adjustments, training and validation loss, and Dice scores according tumor region.
Results: Over the last five epochs, the Physics-Informed ResNetUNet achieved the following scores: Mean Dice of 0.6975, TC Dice of 0.6763, WT Dice of 0.7180, ET Dice of 0.6983, and a training loss of 0.3420 with an average time of 52.44 seconds per epoch. In comparison, SegResNet recorded a Mean Dice of 0.4150, TC Dice of 0.6608, WT Dice of 0.5689, ET Dice of 0.0154, and a training loss of 0.8876 with an average time of 81.53 seconds per epoch. Finally, U-Net achieved Mean Dice of 0.0511, TC Dice of0.0197, WT Dice of 0.1133, ET Dice of 0.0204, and a training loss of 0.9418 with an average time of 41.36 seconds per epoch. Table 1 shows the performance of ResNetUNet and SegResNet in comparison with traditional UNet. Figure 2 shows the performance of the model on training and testing dataset showing the segmented tumor region.
Conclusion: The results demonstrate that the Physics-Informed ResNetUNet outperformed both SegResNet and U-Net in segmentation accuracy, particularly for the Whole Tumor and Enhancing Tumor regions. The incorporation of tumor growth dynamics as an additional layer allows the model to better reflect the physical processes underlying tumor development, leading to a more reliable and precise tool for clinical applications in brain tumor segmentation.
Disclosures: The authors have no conflicts of interest to disclose.
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Poster Presentation

GA161- Physics-informed UNETR: A Brain Tumor Segmentation Combining UNETR Architecture and Physics Constraints Using Brats2021 Dataset and Insights for Molecular Imaging

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Category: Computational & Data Science

Abstract Body:
Background: This Physics-Informed UNETR model incorporates both learned features from MRI scans and the physical constraints of tumor dynamics, offering a more holistic and accurate segmentation. By integrating reaction-diffusion equations, which govern tumor expansion, the model aims to provide more accurate segmentation results, especially in complex cases with irregular tumor boundaries. The problem, therefore, lies in how to effectively combine state-of-the-art deep learning techniques with well-established biological models to improve the accuracy and reliability of brain tumor segmentation. This study seeks to address this gap by developing a novel approach that leverages both