中华医学会放射学分会

2023 年全国分子影像学学术大会

论文汇编

天津

2023 年 06 月

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OR-001

Engineering Cytokine-Potentiated Extracellular Vesicles for Type 1 Diabetes Imaging and Therapy

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Purpose: Extracellular vesicles (EVs) derived from inflammatory cytokine-primed mesenchymal stem cells (MSCs) have been demonstrated with enhanced therapeutic potential in autoimmune disease, such as ulcerative colitis. However, the role and distribution of cytokine-primed MSC-EVs in type 1 diabetes (T1D) remain elusive. The hexyl 5-aminolevulinate hydrochloride (HAL) is the FDA-approved small molecule drug. Herein, we aimed to establish HAL-loaded engineered cytokine-primed MSC-EVs (H@TI-EVs) to exert favorable inflammatory targeting and repair effects for T1D imaging and therapy.

Materials and Methods: Human umbilical cord-derived MSCs at passages three to eight were used in all of subsequent experiments. MSCs were incubated with the medium containing TNF-α, IFN-γ (each at 20 ng/mL) and 10% EV-free fetal bovine serum (FBS) for 48 h. Then the medium supernatant was collected and subjected to a series of differential centrifugation to isolate and purify cytokine-primed EVs (TI-EVs). TI-EVs was examined by transmission electron microscopy (TEM), dynamic light scattering (DLS) and Western blot. Moreover, proteomic analysis was performed to evaluate the protein composition of TI-EVs. HAL molecules were loaded into the TI-EVs via electroporation. 20 μg of HAL and 100 μg of TI-EVs were suspended in an electroporation cuvette at 100 V, 200 Ω and 100 μF. The unloaded HAL was removed by ultrafiltration at 130,000 × g for 2 h to obtain the H@TI-EVs. Then, we determined whether H@TI-EVs can be internalized by a mouse islet β cell line (MIN6 cells) and produce intermediate protoporphyrin (PpIX) of heme biosynthesis initiated by HAL for fluorescence imaging in vitro. The anti-apoptotic and anti-inflammatory effects were also investigated in MIN6 cells and macrophages, respectively. The in vivo performance of HAL and H@TI-EVs were detected in T1D mice via fluorescence imaging. Male C57BL/6 mice were intraperitoneally injected with STZ for 5 consecutive days at a dose of 50 mg/kg body weight to establish a T1D model. Two days after the last STZ injection, free HAL (4 μg) and 100 μg of H@TI-EVs (equivalent to ~4 μg of HAL) were intravenously injected into T1D mice. Then, the time-dependent in vivo distribution of HAL or H@TI-EVs was tracked by PpIX via fluorescence imaging. Furthermore, in vivo therapeutic efficacy of H@TI-EVs in mice with T1D was evaluated via histological analysis and the detection of blood glucose level after four-week therapy. Moreover, plasma insulin levels in different groups of mice were monitored by ELISA kits before sacrifice. An intraperitoneal glucose tolerance test (IPGTT) was performed to further examine the repair ability of H@TI-EVs in mice with dynamic hyperglycemia.

Results: TI-EVs and MSC-EVs presented typical cup-shaped bilayer structures, with a mean size of approximately 120 nm. Both types of EVs were negatively charged with

typical cytosolic proteins and surface markers. The results of proteomic analysis showed that ~545 genes were uniquely upregulated and ~820 genes were significantly downregulated in TI-EVs compared with MSC-EVs (Log2[FC]≥0.5). Proteins related to chemotaxis, proangiogenic effects and anti-inflammatory effects showed markedly increased expression in TI-EVs, indicating the enhanced regenerative ability of TI-EVs. After characterization of the TI-EVs, hydrophilic HAL molecules with anti-inflammatory properties were loaded into the TI-EVs via electroporation to obtain the H@TI-EVs. The expression of marker proteins, size distribution, and zeta potential of H@TI-EVs were not altered compared with those of TI-EVs. Furthermore, we observed colocalization of the red fluorescence of PpIX and the cytoskeletal protein β-tubulin in MIN6 cells, which confirmed H@TI-EVs can be internalized by MIN6 cells. In addition, H@TI-EVs induced the M1-to-M2 macrophage transition and significantly inhibited the protein expression of the apoptosis-related proteins and reactive oxygen species (ROS) generation to exert favorable anti-inflammatory and anti-apoptotic effects. The time-dependent in vivo distribution of HAL or H@TI-EVs was successfully tracked by the fluorescence of PpIX derived from HAL decomposition. Moreover, compared with HAL, more H@TI-EVs targeted and accumulated in the inflamed pancreas due to the ability of TI-EVs to home to the injured pancreas. Quantitative analysis showed that the fluorescence signals of the pancreas in the H@TI-EV group were approximately 2.03-, 2.73-, and 3.30-fold higher than those in the HAL group at 12 h, 24 h and 48 h, respectively. The results of in vivo therapeutic efficacy of H@TI-EVs in mice with T1D illustrated that H@TI-EV treatment significantly prevented the reduction in the islet size and loss of β cells, restored the level of blood glucose and insulin, and enhanced responsiveness to IPGTT, with values similar to those of healthy mice.

Conclusion: We firstly demonstrated H@TI-EVs exerted excellent inflammatory targeting and regenerative effects for T1D imaging and therapy. The accumulated H@TI-EVs in the injured pancreas not only enabled the fluorescence tracking of TI-EVs through the intermediate product PpIX generated by HAL, but also exhibited excellent therapeutic efficiency in T1D mice. This nanosystem has great prospects for clinical translation due to its ease of preparation, feasibility and biosafety.

OR-002

纳米复合体系提高胰腺导管腺癌间质渗透性及 MRI 实时监控研究

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目的：胰腺导管腺癌（PDAC）间质内肿瘤相关成纤维细胞（CAFs）是间质物理屏障建立的关键因素，它限制了临床治疗效果。但是通过消耗 CAFs 促进 PDAC 间质渗透性的策略常因为其不可控性导致令人不满意的结果，因此，一种能打破纤维组织屏障、对肿瘤组织的渗透性进行实时成像的新颖的纳米成像体系是亟须的。

材料与方法：我们构建一种新颖的集间质调节、肿瘤杀伤与无创渗透性监控为一体的多功能纳米体系，此体系由包裹磁性氧化铁的介孔二氧化硅负载 Gemcitabine 和 Fasudil。我们对纳米体系的理化性质、体内外成像能力、PDAC 间质改善能力、肿瘤治疗效果和组织渗透性无创监控能力进行评估

结果：理化性质检测显示 Fe_3O_4-$mSiO_2$ 分散性好，形态均匀，且具有超顺磁性。MR 扫描显示纳米体系具有铁浓度依赖性暗化效应，在细胞内外均具有稳定成像能力。Fe_3O_4-$mSiO_2$-Gem-Fas 处理的 CAFs 细胞 α-SMA、Collagen Ⅰ含量均降低。CCK8 结果显示纳米体系对 PANCO2 细胞有显著凋亡诱导能力。溶血实验、血液生化指标监测以及组织器官形态学检测结果显示纳米体系的生物安全性高。治疗 14d 后 Fe_3O_4-mSiO2-Gem-Fas 治疗组肿瘤组织内有明显的大片状坏死、间质含量降低、组织渗透性显著升高，第一次和最后一次尾静脉注射 Fe_3O_4-$mSiO_2$-Gem 和 Fe_3O_4-$mSiO_2$-Gem-Fas 前后两小时肿瘤内 MR 信号强度差异均具有统计学意义，对应 Fe_3O_4-$mSiO_2$-Gem-Fas 处理组组织内普鲁士蓝的蓝染面积更大。

结论：本研究成功构建 Fe_3O_4-$mSiO_2$-Gem-Fas 纳米复合体系，具有大量载药能力和超顺磁性特性，可以显著抑制 CAFs 细胞内应力纤维的的生成以及胞外间质的重塑，且具有良好的生物相容性及生物安全性。此纳米体系在体内外均具有稳定的铁浓度依赖性的 MR 成像能力，从而实现对肿瘤组织渗透性的实时监测，这种疗效可控的间质调节策略为 PDAC 及相关富间质肿瘤的治疗提供了一种新的治疗思路。

OR-003

自组装的超小 Fe304 纳米粒用于肿瘤靶向双模 T1/T2 加权磁共振成像引导的协同化学动力学和化学治疗

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目的 开发一种新型的自组装超小 Fe_3O_4 纳米团簇，用于肿瘤 RGD（HS-RGD-SH）靶向双模 T1/T2 加权 MR 成像引导的协同化学动力学和化学治疗。

方法 表征合成的纳米粒的形态。3.0-T 临床 MRI 扫描仪测试细胞和肿瘤的 T1 和 T2 弛豫率、MRI 图像和 MR 引导的体内治疗。CCK-8、ROS 染色、EdU 增殖试剂盒和活/死染色验证化疗和化学动力学治疗。记录体重和肿瘤体积。H&E、TUNEL 和 Caspase3 评估治疗后肿瘤组织的变化。

结果 该纳米粒形状均匀，尺寸分布约为 2-8nm，主要尺寸位于 4nm。r1 和 r2 弛豫率分别为 0.296$mM^{-1}s^{-1}$ 和 2.9$mM^{-1}s^{-1}$，r2/r1 值为 9.8。Fe_3O_4-RGD-DOX 组的 T1 成像信号显著增加（162%），T2 成像信号显著减少（53%）。活/死染色和 CCK-8 结果表明，Fe_3O_4-RGD-DOX 可诱导肿瘤细胞死亡，且 ROS 较高。肿瘤大小和体积、H&E、TUNEL 染色和免疫组化显示，Fe_3O_4-RGD-DOX 通过导致细胞凋亡对肿瘤生长表现出显著的抑制作用。主要器官无组织病理学损伤。溶血百分比低于 2%。小鼠的主要血液指标在各组中均无明显变化。

结论 该纳米粒由于合适的尺寸效应和表面丰富的 Fe 离子，具有优异的 T1 和 T2 双模 MRI 能力以及良好的化学动力学治疗能力。在与肿瘤靶向配体 Arg-Gly-Asp（RGD）和化疗药物阿霉素（DOX）结合后，功能化的 Fe_3O_4 纳米粒实现了增强的肿瘤积聚和滞留效应以及协同的化学动力学和化疗功能，为癌症治疗提供了一个强大的治疗平台。

OR-004

18F-PSMA-1007 PET/CT 与 18F-FDG PET/CT 对不同类型脑肿瘤显像的对比研究

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目的 比较 ^{18}F-PSMA-1007 PET/CT 与 ^{18}F-FDG PET/CT 在不同类型脑肿瘤患者中的显像特征及其应用价值。**方法** 前瞻性纳入 2022 年 8 月—2023 年 3 月在我院行 ^{18}F-PSMA-1007 PET/CT 和 ^{18}F-FDG PET/CT 检查的怀疑脑肿瘤拟行术中定向活检或手术的患者 18 例，以病理和随访结果为标准，比较两种 PET/CT 显像对脑肿瘤的诊断效能。通过测量两种不同示踪剂 PET/CT 显像上肿瘤病灶的最大标准摄取值（SUVmax）及病变的肿瘤/背景比（TBR），比较脑肿瘤在 ^{18}F-PSMA-1007 PET/CT 和 ^{18}F-FDG PET/CT 显像中 SUVmax 值和 TBR 值的差别。采用统计学分析方法比较不同示踪剂 PET/CT 成像在肿瘤边界勾画方面的差异。**结果** 18 例脑肿瘤中，有 14 例胶质瘤，2 例淋巴瘤，1 例脑膜瘤，1 例转移瘤。^{18}F-PSMA-1007 PET/CT 诊断胶质瘤的灵敏度和准确性均高于 ^{18}F-FDG PET/CT，差异有统计学意义（$P<0.05$），特异度呈现出高于 ^{18}F-FDG 的良好趋势。病灶在 ^{18}F-PSMA-1007 PET/CT 上的 SUVmax 明显低于 ^{18}F-FDG（$P=0.001$），而 TBR 明显高于 ^{18}F-FDG（$P=0.002$）。^{18}F-PSMA-1007 在脑膜瘤、转移瘤和淋巴瘤病灶中的 TBR 均高于 ^{18}F-FDG PET/CT，而 SUVmax 则相反。此外，^{18}F-PSMA-1007 图像上病灶显示较 ^{18}F-FDG 准确，且肿瘤边界更为清楚（$P<0.01$）。 **结论** 与 ^{18}F-FDG 相比，^{18}F-PSMA-1007 PET/CT 具有较高的 TBR，能更好地显示脑肿瘤病变及其边界，在脑肿瘤评估方面展现出了良好的临床应用潜力。

OR-005

A Fibrin Site-Specific Nanoprobe for Imaging Fibrin-Rich Thrombi and Preventing Thrombus Formation in Venous Vessels

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Venous thromboembolism (VTE) is a prevalent public health issue worldwide. Before treatment, spatiotemporally accurate thrombus detection is essential. However, with the currently available imaging technologies, this is challenging. Herein, the development of a novel fibrin-specific nanoprobe (NP) based on the conjugation of poly(lactic-co-glycolic acid) with the pentapeptide Cys-Arg-Glu-Lys-Ala (CREKA) for selective and semiquantitative imaging in vivo is presented. By integrating Fe3O4 and NIR fluorochrome (IR780), the NP can function as a highly sensitive sensor for the direct analysis of thrombi in vivo. The fibrin-specific NP distinguishes fibrin-rich thrombi from collagen-rich or erythrocyte-rich thrombi, which can be beneficial for future individually tailored therapeutic strategy. Furthermore, loading NPs with the ketotifen fumarate results in mast cell

degranulation inhibition, and hence, NPs can prevent thrombosis without the risk of excessive bleeding. Thus, the use of fibrin-specific NPs may serve as a safe alternative approach for the detection and prevention of VTEs in susceptible populations in the future.

OR-006

Magnetic-optical Dual-modality Monitoring chemotherapy efficacy of Pancreatic Cancer with a Low-dose Fibronectin-Targeting Gd-based Contrast Agent

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Purpose/Background: Pancreatic cancer (PC) is a lethal and hypovascular tumor surrounded by dense stroma, which is recognized as a vital factor of progression. Precise detection and accurate monitoring chemotherapy are important to improve patient survivals. Molecular imaging is a promising method for accurate detection of the disease. Extradomain-B fibronectin (EDB-FN), a high-expression onco-protein in the tumor extracellular matrix, can realize targeted and effective molecular imaging. Here, we prepared EDB-FN targeted Gd-based contrast agent (EDB-Gd-DOTA-IRDye800CW) to perform fluorescence molecular imaging (FMI) and MRI for non-invasive and quantitative imaging and therapeutic monitoring of PC.

Methods: For FMI/MRI, subcutaneous and orthotopic models were established. Mice were intravenously injected with EDB-Gd-DOTA-IRDye800CW and free IRDye800CW or Gd-DOTA at the Gd concentration of 0.05 mmol/kg, merely a half of clinical dose. The TBR (Tumor background ratio) of fluorescence intensity and the ratio of T1 value reduction (T1d%) were compared quantitatively. For chemotherapy monitoring, mice were treated with or without albumin-bound paclitaxel and gemcitabine (AG) chemotherapy regimens. FMI/MRI were performed before and after treatments. Histological analyses were used as references for validation.

Results: The concentration of EDB-Gd-IRDye800CW showed a linear correlation with fluorescence intensity and T1 relaxation time in vitro. The optimal imaging time point was 30min after injection of EDB-Gd-DOTA-IRDye800CW with 0.05 mmol/kg, only a half of clinic dosage, in both FMI and MRI, except FMI of orthotopic model due to limit imaging depth. In addition, the targeted probe generated 1.42-fold and 1.93-fold robust contrast-enhanced and longer retention compared to IRDye800CW or Gd-DOTA ($p < 0.05$). Moreover, AG chemotherapy reduced tumor volume. T1d% and TBR were significantly increased 2.34-fold and 1.31-fold in Vehicle group in fibrotic tumor areas compared to AG group ($p < 0.05$). Histological analyses were used for validation. Additionally, the sensitivity of the EDB-Gd-IRDye800CW could detect tumor diameter of 2mm at 0.05 mmol/kg.

Conclusion: Integration of FMI/MRI with low-dose EDB-Gd-DOTA-IRDye800CW could complement its advantages and visualize PC precisely. Moreover, EDB-Gd-DOTA-

IRDye800CW monitor chemotherapy accurately, which means the targeted probe possesses clinical applications in precise diagnosis, post-treatment monitoring and disease management.

Clinical Relevance/Application: Dual-modality imaging with the targeted probe provided robust enhancement and non-invasive detection of PC compared to clinical standard contrast agents, Gd-DOTA. The optimal imaging dosage of the targeted probe is only half of dosage of gadolinium for clinical use, which allows for more safe and efficient imaging examination for patients. Moreover, the targeted probe can noninvasively and quantitatively measure fibrotic changes in the tumor bed after chemotherapy, which traditional imaging techniques based on RECIST 1.1 are difficult to distinguish, and help with accurate diagnosis and staging, treatment monitoring and disease management in the future.

OR-007

Manganese Ion-Bridged Nanodrug for MR/NIR-I/II Fluorescence Imaging and Synergistic Phototherapy of Breast Cancer

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As an emerging anticancer approach, photodynamic therapy (PDT) produces cytotoxic reactive oxygen species (ROS) by exciting photosensitizers (PSs) under light triggers in the tumor site, which has the advantages of minimal invasiveness, fewer side-effects, and negligible drug resistance. However, the therapeutic efficacy of PDT is still stunted by several intrinsic obstacles, such as shallow depth of light penetration, tumor hypoxia and inevitable phototoxicity. Herein, we successfully developed a carrier-free nanodrug, IR820-Mn/TH287, based on coordination-driven self-assembly of IR820/TH287 with Mn^{2+} via a "green" method. Photophysical properties of IR820-Mn/TH287 exhibited J-aggregates of IR820 monomer, such as absorption/emission beyond 900 nm, enhanced absorption coefficients, and photothermal performance. Molecular dynamics simulations further illustrated the interaction between Mn^{2+} and IR820 during the formation process of J-aggregates. Under laser irradiation, IR820-Mn could produce higher photothermal temperature and sufficient ROS to cause oxidative damage, and TH287 could improve cellular sensitivity to oxidative damage by suppressing the activity of MTH1 protein. Furthermore, the best time for laser irradiation would be achieved under the precise guidance of MR/NIR-I/NIR-II fluorescence imaging. Because of the synergistic effects from the above designs, IR820-Mn/TH287 could hold high-efficiency tumor elimination with negligible toxicity. Such Mn^{2+}-coordinated carrier-free nanodrug with multimodal imaging-guided phototherapy in NIR-II window could be an efficient and safe approach for breast cancer treatment.

OR-008

Oxygen Self-Supplying Nanosystem Utilizing Radiation and Dual-Enzyme Mechanisms for Enhanced Tumor Radiotherapy Sensitization and Imaging

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Objectives: Hypoxia is a condition frequently observed in solid tumors caused by abnormal tumor blood vessels, excessive tumor cell proliferation, and an aberrant lymphatic system. Previous research has demonstrated that tumor hypoxia is a significant factor contributing to the failure of tumor therapy. Oxygen is essential for generating reactive oxygen species that kill tumors during radiotherapy, and therefore, the hypoxic tumor microenvironment is a common cause of radiotherapy resistance. Numerous strategies have been proposed recently to reverse tumor hypoxia and improve the outcomes of radiotherapy. However, no effective oxygen donor is currently available for clinical use to alleviate tumor hypoxia. This study aims to construct a novel cyclic self-oxygenating nanosystem by co-loading catalase (Cat) and superoxide dismutase (SOD), which can continuously and efficiently produce oxygen from water molecules in tumor tissues under the "initiation" of radiation, thereby enhancing the therapeutic effect of tumors. Photoacoustic imaging and fluorescence imaging techniques are used to monitor the oxygen content in tumors and the in vivo biological distribution of the nanoplatforms in real time, providing further guidance for mouse radiotherapy.

Methods: The core structure of this nanosystem consisted of a degradable hollow hybrid organosilica nanoparticle (HSN), which encapsulated catalase (Cat) and superoxide dismutase (SOD) enzymes (SC@HSN). The nanoparticle was then coated with a zeolitic imidazolate framework-8 (ZIF-8) metal-organic framework that carried NIR-I fluorescent dyes (SC@HSN@Z-F). The characterization of this nanomaterial was conducted through transmission electron microscopy, Zeta potential, X-ray diffraction, and dynamic light scattering. The oxygen production of nanoparticles under X-ray stimulation was measured using an oxygen detection probe $[Ru(DPP)_3]Cl_2$. The expression level of HIF-1α was assessed through Western blot analysis and immunofluorescence experiments. The cytotoxic effects of nanoparticles on tumor cells were evaluated using the MTT assay. In addition, an in situ breast cancer model was established, and the biodistribution of nanoparticles was monitored in real-time using near-infrared fluorescence imaging. The therapeutic efficacy was assessed by tracking changes in tumor volume and survival period analysis.

Results: The nanosystem targeted tumor tissues through the enhanced permeability and retention (EPR) effect. Within the acidic tumor microenvironment, ZIF-8 underwent degradation, releasing NIR-I fluorescent dyes suitable for fluorescence imaging. Concurrently, the hollow hybrid organosilica experienced degradation upon interaction with glutathione (GSH), leading to the release of the two enzymes. Upon initiation of

radiotherapy, ionizing radiation generated reactive oxygen species (ROS) from water molecules, including superoxide anions (O^{2-}). The superoxide anions were then converted to hydrogen peroxide (H_2O_2) under the catalytic action of SOD. Subsequently, oxygen was produced via the catalysis of Cat acting upon H_2O_2. The TEM image showed that SC@HSN@Z-F NPs were about 50 nm. The results of the in vitro experiments demonstrated that SC@HSN@Z-F nanoparticles exhibited potent anticancer properties. The results of the in vivo experiments confirmed the in vivo distribution and anticancer efficacy of these nanoparticles.

Conclusions: This innovative nanosystem facilitated the continuous generation of oxygen from water molecules within tumor tissues upon exposure to external radiation, ultimately ameliorating the tumor microenvironment and enhancing the sensitivity of tumors to radiotherapy.

OR-009

Multifunctional nanomedicines-enabled chemo/sonodynamic-synergized multimodal tumor imaging and therapy

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Objectives: Nanotechnology-based systems have emerged as a promising paradigm for integrating biomedical imaging and cancer treatment modalities. Owing to their exceptional safety and specificity, these nanomaterials facilitate in situ delivery of imaging probes and the transformation of less harmful substances into potent antineoplastic agents, as triggered by the unique tumor microenvironment (TME). Nonetheless, the intrinsic antioxidant mechanisms and inadequate levels of hydrogen peroxide (H_2O_2) in neoplastic cells considerably impede their effectiveness. The employment of nanozyme-mediated glycolytic reactions, serving as a highly efficient catalyst for H_2O_2 generation, may address these limitations by supplying exogenous H_2O_2, thereby augmenting the impact of reactive oxygen species (ROS)-based chemotherapy. In this context, our objective is to develop a nanotechnology-driven system designed to bolster the efficacy of combined chemo/sonodynamic cancer therapy, while concurrently facilitating efficient imaging.

Methods: In this study, a novel methodology was developed by integrating glucose oxidase (GOx) into the nucleus of biodegradable hybrid hollow silica nanoparticles (HSN) and encapsulating them within the metal-organic framework (MOF) known as HKUST-1, which encompassed a luminescent dye and sonosensitizer TCPP (designated as GOx@HSN@HKUST-1-TCPP). Characterization of this nanomaterial was conducted through transmission electron microscopy, Zeta potential, X-ray diffraction, and dynamic light scattering. The cytotoxic effects of nanoparticles on tumor cells were evaluated using the MTT assay. In addition, an in situ breast cancer model was

established, and the biodistribution of nanoparticles was monitored in real-time using near-infrared fluorescence imaging. The therapeutic efficacy was assessed by tracking changes in tumor volume and survival period analysis.

Results: Through the enhanced permeability and retention (EPR) effect, GOx@HSN@HKUST-1-TCPP efficiently accumulated at the tumor site following systemic administration. Within an acidic tumor microenvironment (TME), the external layer of the pH-responsive HKUST-1 underwent rapid degradation, expediting the release of Cu^{2+} and TCPP. The Cu^{2+} ions interacted with intracellular glutathione (GSH) to dismantle the reactive oxygen defense mechanisms and were reduced to Cu^{+}. Concurrently, the inner layer's GOx@HSN underwent swift biodegradation, liberating GOx, which could be catalyzed to yield H_2O_2 and gluconic acid. The generated H_2O_2 further engaged with the acquired Cu^{+} to initiate a highly efficient Fenton-like reaction, producing hydroxyl radicals (•OH) for enhanced chemodynamic therapy (CDT). Additionally, the liberated TCPP functioned as both a luminescent dye and a sonosensitizer, facilitating effective sonodynamic therapy (SDT) and tumor imaging.

Conclusions: GOx@HSN@HKUST-1-TCPP nanoparticles possessed a robust anticancer effect and offered a reliable breast cancer imaging and therapy platform.

OR-010

Ferroptosis and Autophagy -Inducing and GSH Responsive T1/T2 Dual-modal MR Imaging Bioactive Multifunctional Hollow Nanocomposites for Tf Targeted Breast Cancer Synergistic Therapy

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Objective: To investigate the effect of simultaneously tracking drug release and penetration within the tumor by GSH responsive T1/T2 dual-modal MR imaging and the mechanism of GSH elimination functions for enhancing breast cancer diagnosis and combined therapeutic efficiency.

Methods: The $hMnO_x$ hollow nanoparticles were synthesized with $MnCl_2 \cdot 4H_2O$, sodium oleate. The obtained manganese oleate complex was added with 250 mL octadecene and mixed well. The mixture solvent was heated to 320 ℃ for 30 minutes. Then the obtained manganese oxide nanoparticles were further modified with DMSA and conjugated with transferrin and DOX. The morphology, crystal structure, atomic valence state, Fourier transform infrared (FTIR),ultraviolet-visible (UV-vis) light absorption spectra, element quantification and distribution, zeta potential value and relaxation rate, and MRI images have been detected to characterize obtained nanoparticles. The tumor targeting ability of $hMnO_x$-Tf nanoparticles was assessed by confocal laser scanning microscope, flow cytometry and ICP-MS in vitro and vivo. The cell counting kit-8 (CCK-8) and cell

proliferation assay were used to evaluate the cytotoxicity assessment in vitro. The expressions of cleaved-caspase3, p62, LC3B and GPX4 proteins were evaluated in vitro. The intracellular GSH, reactive oxygen species (ROS) and lipid ROS content were used to detect the cell ferroptosis. The tumor volume, mice weights, tumor sizes, H&E, cleaved-caspase3, GPX4, LC3B. Ki67 and TUNEL stains were used to investigate the therapeutic effects of hMnOx-DOX-Tf in vivo.

Results: The results show that the Mn, O, and S elements uniformly distribute in the hMnOX-DMSA nanoparticle. There Mn^{2+}, Mn^{3+}, and Mn^{4+} exist simultaneously, indicating that the DMSA modification process would induce the oxidization of the hMnOX nanoparticles. The T1 and T2 relaxation rate (r1 and r2) of $hMnO_x$-DMSA was 0.49 and 0.8 mM/s in the group that did not contain GSH, while the relaxation rate with GSH (10mM) reached 4.02 and 20.22 mM/s. T1 Weight imaging signal intensities of 4T1 cells in the group of $hMnO_x$-Tf were significantly higher and the T2 weighted imaging was much darker. The tumor tissue of 4T1 tumor-bearing BALB/c mice showed brighter signal intensities on T1WI and darker signal intensities on T2 WI after injection of $hMnO_x$-DOX-Tf nanoparticles. After incubation with $hMnO_x$-DMSA, $hMnO_x$-Tf and $hMnO_x$-DOX-Tf of GSH level were 75.84 ± 8.45%, 58.8 ± 8.15%, 85.13 ± 2.85% and 37.07 ± 8.63%. Intracellular ROS and lipid ROS were increased after incubation with $hMnO_x$-DOX-Tf. Interestingly, the $hMnO_x$-DOX-Tf group showed the most down-regulatory effect on the GPX4 level, and the cleaved caspase-3 level, p62 and LC3B were obvious up-regulation. The viability of 4T1 cells and the number of proliferating cells after treatment with hMnOx-DOX-Tf is strikingly lower than that treated with DOX. After treatment with hMnOx-DOX-Tf, the tumor volume, H&E, cleaved-caspase3, GPX4, Ki67 and TUNEL stain results showed the excellent antitumor effect of the combination therapy.

Conclusions:

GSH responsive targeted hMnOx-DOX-Tf realized allows treatment of tumor, real-time T1/T2 dual-modal enhancing MR imaging monitoring of drug delivery and release in vivo, and evaluation of treatment efficacy for BC. The Tf-targeted MR imaging enhanced the tracking of drug release and penetration by increase hMnOx-DOX-Tf accumulation in tumor cells. After exhausting GSH and increasing ROS of intracellular, ferroptosis and autophagy antitumor efficiency has enhanced. In addition, hMnOx-DOX-Tf can be used to exert antitumor affection and enhance chemotherapy efficiency by induced ferroptosis and autophagy in vitro and vivo. More importantly, this study revealed GSH responsive nanoparticles could be a great carrier to monitor tumor treatment and enhance synergistic therapeutic efficiency.

OR-011

血清浓度诱导的四氧化三铁纳米粒表面蛋白冠动态演进重塑细胞代谢

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四氧化三铁（Fe_3O_4）纳米粒在磁共振分子影像探针、肿瘤纳米诊疗等临床前研究阶段均表现出巨大潜力，但其体内外生物学效应的差异限制了其进一步临床转化。研究发现纳米材料能吸附周围环境中的蛋白并在其表面形成一层冠状物（蛋白冠），从而将纳米材料由化学界面转变为生物学界面，体外细胞培养环境与体内血液环境存在巨大差异，这一差异将导致纳米粒在体内外环境下形成不同的蛋白冠，进而导致体外培养细胞和体内细胞具有不同的生物学行为。本研究拟体外模拟制备体外、体内两种环境下形成的“Fe_3O_4-血清蛋白”复合物，进一步与溶酶体和细胞质蛋白反应制备“Fe_3O_4-血清-胞内蛋白冠”复合物，并利用 Lable-free 蛋白质组解析蛋白冠的组成，同时分析了上述两种蛋白冠复合物对 J774A.1 细胞转录水平的影响。结果显示，将 Fe_3O_4 纳米粒分别与 10%血清和 50%血清的模拟液体共孵育成功制备了两种“纳米-蛋白冠”复合物（Fe_3O_4@10%B 和 Fe_3O_4@50%B），细胞水平的内吞结果显示，与裸纳米粒相比，蛋白冠的形成均降低了其被 J774A.1 细胞的内吞；进一步内吞途径研究显示，裸的 Fe_3O_4 纳米粒主要以大胞饮的方式被巨噬细胞 J774A.1 摄取，而 Fe_3O_4@10%B 以小窝蛋白和网格蛋白介导的内吞为主，Fe_3O_4@50%B 则主要以大胞饮为主；Fe_3O_4@10%B 和 Fe_3O_4@50%B 的 Lable-free 蛋白质组分析显示，两种复合物中存在大量丰度差异的蛋白，这些差异蛋白包括调理素蛋白及抗调理素蛋白，这些蛋白丰度的差异导致了上述内吞行为的差异。两种蛋白冠处理细胞后的转录组分析结果显示，Fe_3O_4@10%B 和 Fe_3O_4@50%B 处理 J774A.1 细胞后，其补体活化和蛋白激活级联调控等通路发生了显著性改变。本研究从纳米材料体内外测试所处环境的差异出发，探究了体内外血清浓度差异这一关键点对“纳米-细胞”反应的影响，并从蛋白冠的组成解析了其具体机制，本研究为进一步推动纳米材料的体内应用提供了相关理论基础。

OR-012

A dual-modal MRI/NIR fluorescent imaging probe for glioblastoma diagnosis

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Introduction: Glioblastoma (GBM) is the most common primary malignant tumor in the central nervous system. The current standard treatment strategy for GBM consists of the maximal safe surgical resection followed by radiotherapy (RT) and chemotherapy. However, high risks of disease recurrence and metastasis could lead to a poor prognosis of GBM due to residual disease after the surgery. Therefore, accurately determining the margin of the tumor could benefit the surgeon in rationally and completely removing the tumor, and thus improve the prognosis of GBM.

Magnetic resonance imaging (MRI) is one of the most important imaging diagnostic techniques for GBM. Nonetheless, due to GBM's unique intracranial tumor localization, the non-specific gadolinium (Gd)-based contrast agents often used clinically generally cannot cross the blood-brain barrier (BBB) into intracranial tumor tissue, resulting in that more than 10% of GBM cannot be discriminated by enhanced MRI. Therefore, it is imperative to find a novel MRI contrast agent for GBM imaging.

Superparamagnetic iron oxide nanoparticles (SPIONs) serve as paramagnetic MRI contrast agents, which could be used for multimodal imaging without the limitations of a single imaging technique. Considering that transferrin receptors (TfR) that are highly expressed in the BBB and brain tumor tissues could be used to deliver probes to the brain for targeting GBM, nanoprobes that target the TfRs with high affinity and high stability were constructed based on the multi-modal imaging strategy.

Methods: First, we used the standard solid-phase synthesis method to synthesize ^{D}THR(Ac-pwvpswmpprht-COOH, the reverse enantiomer of THR (one of the ligands of TfR), to improve the stability of THR during circulation in vivo). SPIONs were synthesized by the thermal decomposition method and were subsequently wrapped by ^{D}SPE-PEG(2000)-amine for surface modification. Then, SPIONs were used as the nanoplatforms to combine near-infrared (NIR) fluorescent dye Cy7 with ^{D}THR to construct a MR/NIR dual-modal nanoprobe (^{D}THR/Cy7-PEG-DSPE-SPION). Second, the quantitative grafting ratio of the ^{D}THR peptide was examined by an ultraviolet spectrophotometer; the connection of NIR dyes and SPIONs was determined by a microplate reader; the morphology, size distribution and electrical properties of the probes were characterized by transmission electron microscopy (TEM), dynamic light scattering (DLS) and selected area electron diffraction (SAED); MR images were acquired using a 3.0 T MR scanner, and T_2 relaxation time were calculated. Besides, we examined cytotoxicity in vitro using CCK-8, and the cell labeling efficiency and intracellular distribution of ^{D}THR/Cy7-PEG-DSPE-SPION were separately evaluated by flow cytometry and NIR fluorescence imaging microscopy, and construction in vitro BBB model and the permeability of probes BBB was investigated by transwell experiment. Finally, we constructed GBM model in situ, evaluated its capabilities in MRI and NIR imaging and the distribution of probes in mice by ICP-MS.

Results: An evident decreased absorption in the UV-vis spectrum at approximately 280 nm indicates decreases in amino acids after coupling, which confirmed that ^{D}THR peptide was successfully attached to the NH_2-PEG-DSPE-SPION. Meanwhile, a multifunctional fluorescence microplate reader shows an excitation peak at 720 nm and an emission peak at 820 nm for ^{D}THR/Cy7-PEG-DSPE-SPION , which indicates the successful conjugation of Cy7. DLS measurement, TEM image shows that the diameter of ^{D}THR/Cy7-PEG-DSPE-SPION nanoprobe is approximately 10 nm. T_2 relaxation were measured with a 3.0 T MRI scanner, and the r_2 values of ^{D}THR/Cy7-PEG-DSPE-SPION were 121.4 S^{-1} mM^{-1}, demonstrating that they are appropriate for highly effective T_2-weighted MR imaging. Besides, the results of CCK-8 shows a low cytotoxicity of the nanoprobe. Flow cytometry and NIR fluorescence imaging microscopy exhibit that untreated and pretreated ^{D}THR/Cy7-PEG-DSPE-SPION can be effectively internalized by U87-MG cells and bEnd. 3 cells. Importantly, transwell experiments show that the material can effectively cross the BBB. Finally, MRI image demonstrated that the targeting nanoprobes could achieve the targeting of brain tumor via the TfR mediated

BBB penetration and thereby enhance the MR contrasts of GBM. The heterogeneous signal enhancements of the fluorescent signals suggest that the nanoprobes could accumulate in the tumor center and margin, and thus ^{D}THR/Cy7-PEG-DSPE-SPION probes can accurately characterize the tumor margin . ICP-MS results show that the probe could be metabolized by liver and thus demonstrates a good biocompatibility.

Conclusion: In recent years, the application of multi-modality imaging in the field of neuroscience has gradually attracted the attention of clinicians because it can overcome the limitations of a single imaging mode and improve the specificity and sensitivity of imaging. In this study, ^{D}THR/Cy7-PEG-DSPE-SPION nanoprobes show a high efficiency of MR imaging and near-infrared fluorescence imaging, reflecting ^{D}THR retains the main functions of THR and has a high stability against protease in the circulation and an ability to cross the BBB and target gliomas sites. Meanwhile, it has a longer circulation time and has a low biotoxicity. All the experimental results show that our peptide modification and the structure of the overall imaging agent have fully exerted their respective functions. Consequently, this novel nanoprobe has the potential to stand out in the next generation of targeted glioma contrast agents and we believe that this success will make a significant contribution to the preoperative diagnosis and the intraoperative localization of glioma.

OR-013

癌细胞膜包覆的纳米颗粒用于 PA/MR 多模态成像

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目的：目前，癌症仍严重危害着人类的健康。精准医学为临床肿瘤诊断提供了新思路。其中，成像将肿瘤大小位置可视化，用于治疗前制定精确的方案，以及治疗效果评价。磁共振成像作为一种无创、无电离辐射的成像技术，得到了广泛应用，但灵敏度较低。光声成像是一种新兴的无创成像方法，具有高灵敏度和组织分辨率，有着良好的肿瘤诊断效果。因此，我们研究了一种癌细胞包覆的多模态成像纳米探针，可精准靶向乳腺癌，用于其诊断。

方法：（1）通过共沉淀法合成了 Fe_3O_4 磁性纳米粒子,并用柠檬酸对其进行修饰，通过一锅法在其表面生长 MnO_2，得到产物 Fe_3O_4@MnO_2（简称 FM）。癌细胞膜通过超声法包覆在 FM 表面，得到 Fe_3O_4@MnO_2@CM（简称 FMC）。通过透射电子显微镜、纳米粒度仪观察纳米颗粒的形态和大小。在模拟生理环境和肿瘤微环境下验证 FMC 纳米探针的磁共振和光声成像效果。

（2）构建了 4T1 小鼠皮下肿瘤模型，并分为 PBS、FM、FMC 组。尾静脉注射 PBS、FM、FMC 后在不同时间点进行磁共振和光声成像，确定药物在肿瘤部位的达峰时间，对 FMC 纳米探针的多模态成像效果进行评价。

结果：（1）FMC 纳米探针基本表征结果：透射电镜下和粒度仪观察到 FMC 纳米探针大小均一，分散均匀。磁共振和光声成像结果显示，FMC 纳米探针在体外具有良好的 T1-T2 双对比和光声成像效果。

（2）小鼠体内实验结果：体内磁共振成像结果显示，尾静脉注射 8h 后，药物在肿瘤的浓度达到峰值，PBS 组信号无明显变化。并且 FMC 组的 T1 信号比 FM 组亮，T2 信号则暗于 FM 组，表明由于癌细胞膜的同源靶向性，FMC 组在肿瘤部位的药物富集程度高于 FM 组。光声成像结果与磁共振结果一致，表明该探针具有良好的磁共振和光声成像效果及靶向性。

结论：FMC 纳米探针在体外和体内均具有良好的磁共振和光声成像性能，可用于精准影像学指导，为临床精确诊断乳腺癌提供了新思路。

OR-014

Development of F-18-labeled acridone analogues for PET imaging of STING

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Objectives: Stimulator of interferon genes (STING) is a critical protein serves as a mediator for pivotal downstream of cyclic guanosine monophosphate-adenosine monophosphate synthase (cGAS). The activation of the cGAS-STING pathway has tremendous potential to improve anti-tumor immunity by generating type I interferons. Previous efforts on STING-targeted radioligand have been published with dimeric amidobenzimidazole core[1]. The relevant studies on [^{18}F]F-CRI1 were reported in iSRS2022[2], here we developed another two acridone analogues with 2-3 PEGs for increasing hydrophilicity and improving metabolism performance.

Methods: [^{18}F]F-CRIn (n = 1, 2, 3) was successfully synthesized and octanol/water partition coefficient (logP) was experimental measured. The affinity of the probes to STING were obtained by cell saturation assay. *In vivo* PET imaging was performed on B16F10 tumor-bearing mice. Furthermore, the tumor-to-muscle (T/M) ratios and tissues uptake were analyzed.

Results: The logP of these probes was measured as 1.68 ± 0.03, 1.03 ± 0.07 and 1.04 ± 0.04, respectively, which was gradually decreased as the increase of PEG chain. Similarly, the Kd value of these probes were 40.62 nM, 102.3 nM and 207.8 nM, respectively. B16F10 tumors were visualized within 30 min with T/M ratios 2.31 ± 0.31, 2.15 ± 0.14 and 2.27 ± 0.21, which showed no significant difference after data analysis. Besides, compared with [18F]F-CRI1, the uptake of [18F]F-CRI3 in the intestines and gallbladder were significantly decreased which may be a result of hydrophilia increase of the structure (52% decreased for intestines and 62% for gallbladder). [^{18}F]F-CRI2 presented a middle performance in the above experiments with a reduced background signal while maintained moderate affinity.

Conclusions: All of the radioligand showed well T/M ratios (range from 2.00 to 2.62), and structure modification strategy effectively reduced the uptake at the biliary-intestinal tissue to have a better imaging contrast. Collectively, these ^{18}F-labeled small molecules showed promising potential for in vivo noninvasive STING visualization in tumors, among which [^{18}F]F-CRI2 showed the best comprehensive performance.

Acknowledgments: This study was financially supported by the Major Research Plan of the National Natural Science Foundation of China (91959122), National Natural Science Foundation of China (81901805, 21976150), Joint Fund of the National Natural

Science Foundation of China - China National Nuclear Corporation for Nuclear Technology Innovation (U1967222).

References: [1] Fang J, Feng L, Meng L, Wang X, Liu H, Huang L, et al. A novel ^{18}F-labeled agonist for PET imaging of stimulator of interferon gene expression in tumor-bearing mice. Eur J Nucl Med Mol Imaging 2022;50:27-37.

[2] Liu HH, Li JD, Fang JY, Feng LX, Yang HZ, Li JC, et al. Development of F-18-labeled agonist for imaging STING in the tumor microenvironment. Nucl Med Biol 2022;108:S19-S20.

OR-015

Novel STING-targeted PET tracer for inflammation imaging

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Objectives: Inflammation, as a part of innate immunity, plays an important role in host defense and participates in cell recovery and regeneration. Stimulator of interferon genes (STING) is a key molecular biomarker of innate immunity in response to inflammation, and can be used as an imaging biomarker for early diagnosis and prognosis evaluation of inflammation. Many diseases occur and develop through STING activation, such as acute lung injury (ALI), myocarditis, rheumatoid arthritis and atherosclerosis etc. To achieve accurate non-invasive diagnosis of inflammation-related diseases, ^{18}F was used to label a STING agonist-benzothiophene derivative, and a novel STING-targeted radiotracer, [^{18}F]FBTA, was obtained. PET imaging was used to evaluate the relationship between the intensity of radiation signal and the expression of STING in inflammation-related diseases for early diagnosis.

Methods: ALI and myocarditis mouse models were induced by administration of lipopolysaccharide (LPS) and porcine cardiac myosin respectively in Balb/c mice, while another group of mice were treated with saline as controls. The tosylate precursor was labeled with ^{18}F and then reacted with TFA to produce [^{18}F]FBTA. Dynamic PET/CT was performed after intravenous injection of [^{18}F]FBTA. *Ex vivo* biodistribution of [^{18}F]FBTA was determined by a γ-counter. The inflammation level was assessed by measuring the expression of STING and other inflammatory markers in the tissues by immunohistochemistry or flow cytometry.

Results: [^{18}F]FBTA was obtained in high radiochemical yield (70%-80%), high radiochemical purity (> 99%) and high molar activity (32.5 ± 2.9 GBq/μmol). In ALI mice, intratracheal LPS instillation led to an acute inflammatory response in the lungs, characterized by increased expression of MPO and STING, along with a significant increased [^{18}F]FBTA uptake in inflammatory lesion of lungs. Compared with the control group, PET-derived data showed that the ALI mice had a significant radioactive accumulation in lung lesions, and the more severe the ALI, the higher the radioactive enrichment. The uptake of lung lesions (15.96 ± 0.62 %ID/g) and

lung to muscle ratio (10.62 ± 2.67) reached the maximum in the ALI-24 h group. There was a strong correlation between the LPS induce time and [^{18}F]FBTA uptake, as quantified by *in vivo* PET (R^2=0.94). The *ex vivo* biodistribution studies of [^{18}F]FBTA were almost consistent with the PET imaging results. In mice with myocarditis, [^{18}F]FBTA-PET revealed significantly higher [^{18}F]FBTA uptake in the inflamed myocardium (***P < 0.001), consistent with markedly increased STING expression in the inflammatory lesions. Moreover, [^{18}F]FBTA-PET imaging data also showed the heart to muscle ratio in mice with myocardium was significantly higher than controls (***P < 0.001). The biodistribution studies confirmed the noninvasive imaging of PET/CT, and flow cytometry results verified the infiltration of macrophages in heart is the main reason for the increase of STING expression in myocardium.

Conclusions: A novel STING-targeted PET tracer, [^{18}F]FBTA, was synthesized with high radiochemical yield and high molar activity. [^{18}F]FBTA successfully tracked inflammation in mice, such as ALI and myocarditis, and was proved to be a robust quantitative method for imaging of innate immune responses, which makes it a potential candidate for clinical translation.

OR-016

新型双模态纳米影像探针用于脑胶质瘤的精准诊断

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目的：利用纳米技术制备一种同时具有化学交换饱和转移和超声造影特性的双模态纳米影像探针（PEG-PLLA@SA・PFP），有望实现结构与功能成像的有机融合，进而达到对脑胶质瘤的精准诊断。

方法：采用开环聚合方法合成一种新型嵌段共聚物聚乙二醇-L-聚乳酸（PEG-PLLA）纳米颗粒载体。采用乳化-溶剂蒸发法将水杨酸（salicylic acid, SA）和全氟戊烷（perfluorinated pentane, PFP）装载到纳米颗粒载体 PEG-PLLA 内，进而制备一种新型双模态纳米影像探针（PLLA-HP@SA・PFP）。通过氢核磁共振谱（1H-NMR）、透射电镜、粒径仪、CCK8 试验、细胞划痕试验、血液生化分析等方法对合成的纳米颗粒体系进行多尺度评价。构建脑胶质瘤动物模型，利用超声成像和化学交换饱和转移（CEST）成像技术对 PEG-PLLA@SA・PFP 纳米探针的成像效果进行综合评价。

结果：1H-NMR 表明 PEG-PLLA 聚合物纳米颗粒制备是成功的。细胞实验和活体实验表明 PEG-PLLA 纳米颗粒无毒，具有良好的生物相容性。TEM 和 DLS 显示 PEG-PLLA@SA・PFP 平均粒径和 Zeta 电位分别为 223.8 ± 2.5 nm 和-39.6 ± 1.9 mV。试管实验、动物实验表明 PEG-PLLA@SA・PFP 纳米颗粒同时具有 CEST 和声学特性，可用于增强图像对比度和成像灵敏度。与注射前基线图像比较，注射后 105 min 纳米探针 PEG-PLLA@SA・PFP 在肿瘤内显著积聚。

结论：我们成功制备一种新型双模态纳米影像探针 PEG-PLLA@SA・PFP，这为今后造影剂的开发和最终实现肿瘤的精准影像诊断具有重要指导意义。

OR-017

活体比率成像

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在活体层面对疾病特征分子的实时动态变化信息进行成像及测量，这对于研究疾病发生分子机制具有重要意义每种活体成像技术都各具独特的优势和固有的局限性，近红外二区（NIR-II，950-2000 nm）的荧光成像的灵敏度十分优异，但组织穿透力和在浑浊介质中的空间分辨率较低；NIR-II 区的光声成像的空间分辨率较好、穿透深度深，但是灵敏度很有限。 因此，如何设计分子探针，集成这两种二区成像，实现优势互补的双模式增强，是肿瘤微环境分子影像的材料科学问题，但相关材料仍然缺乏发展与报导。为进一步提高活体成像精准度及实现可定量分析，我们课题组发展了一系列具有响应性的 NIR-II 区荧光与光声双模式成像比率分子探针，用于靶向成像具有免疫检查点通路的肿瘤细胞以及免疫相关细胞的特征生物标记物。同时建立了基于 NIR-II 区比率型成像的活体测量新的方法，提高了对生理分子信息原位、定量获取的精准度。进一步揭示了活体分子比率成像信号与疾病发生发展之间的关联机制，提出了实时、无创疾病活体分子诊断新策略。

OR-018

具有 T1-T2 双模式 MR 成像的新型纳米酶探针在肿瘤治疗和成像中的应用

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目的：纳米酶在肿瘤治疗过程中具有巨大潜力。在这项工作中，拟构建一个由 Cu、Mn 和 Fe 掺杂的多金属纳米酶（Polymetallic nanozyme）探针。该探针同时具有磁共振 T1-T2 成像能力，在小鼠尾静脉注射后可以有效富集到肿瘤区域，从而更好地监测指导酶催化的肿瘤疗法，抑制肿瘤细胞生长。材料与方法：利用共沉淀法合成具有高催化效率的纳米探针 $Cu_{0.5}Mn_{0.5}Fe_2O_4$（简称 CMF）并对其进行表面修饰；通过表面静电吸附牛血清白蛋白（BSA）增加纳米酶的水溶性和稳定性，完成新型 CMF@BSA 纳米酶的组装。纳米酶经过透射电镜、便携式溶解氧测定仪、紫外-可见光光谱、动态水合粒径和磁共振成像等进行基本表征以及酶特性的研究。体外细胞实验验证 CMF 纳米酶的毒性、产生活性氧（ROS）情况以及增强线粒体膜电位的损伤效果。体内实验验证 CMF 纳米酶的特异性成像能力以及治疗效果。结果：透射电镜、紫外-可见吸收光谱等结果表明了 CMF 纳米探针的成功制备。在 pH=5.4 的反应环境下，CMF 具有良好的产 ROS 性能。磁共振表征结果显示 CMF 具有良好的 T1-T2 双对比成像效果。CCK-8 实验和活死细胞染色证实了 CMF 在较低的浓度下具有良好的肿瘤杀伤效果，在给予超声增强治疗后对肿瘤细胞的生长具有进一步的显著抑制作用。体内实验结果表明，该纳米酶具有 MRI T1-T2 的高效成像能力，表明 CMF 是一种很有前景的磁共振对比剂。结论：CMF@BSA 纳米酶探针作为一种多金属多酶活性的纳米探针，可在肿瘤细胞内产生显著的 ROS，提高酶催化治疗效果，在肿瘤成像和肿瘤生长抑制方面具有很大的应用潜力。

OR-019

放射纳米医学--放射增效探针功能设计和肿瘤诊疗研究

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“高精度、低剂量、高疗效、低损伤”是肿瘤放射影像诊断和放射治疗长期追求的目标。为了实现这一目标，近五年来，申请人围绕“放射功能探针多模态影像与高效治疗”关键科学与技术问题，从提升探针稳定性、增强性能角度出发，以磁共振造影剂和低剂量放疗策略为主要研究对象，深入系统发展了系列放射响应探针：（1）创新提出碳化层锚定方法，成功制备高稳定、高性能的 T1 加权磁共振造影剂，并引入光疗和放射功能，有效弥补了临床线性钆配合物磁共振造影剂稳定性和性能的缺陷。（2）创新发展了辐射发光实时转化的低剂量肿瘤放疗新策略，低剂量放疗有效抑制深层辐射耐受性肿瘤，成功降低临床放疗使用高辐射剂量引发的高毒副作用。

代表性论著（只标注通讯作者）

1. Hongmin Chen*. Nature Commun. 2022, 13, 1938 (IF 17.694).
2. Zhongfu An*, Hongmin Chen*, Wei Huang*. Nature Commun. 2022, 13, 5091 (IF 17.694).
3. Hongmin Chen*. Nucleic Acids Res. 2023, In Press (IF 19.160). https://doi.org/10.1093/nar/gkad178
4. Xiaoyuan Chen,* Hongmin Chen*. Angew. Chem. Int. Ed. 2020, 59, 9914 (IF 16.823).
5. Xiaoyuan Chen*, Hongmin Chen*. Adv. Mater. 2020, 32, 2000377 (IF 32.086).

OR-020

基于新型 MRI/NIR-II/PAI 多模态有机分子探针的合理设计在中晚期肝癌术前降期及成像引导手术切除评价中的应用

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目的：针对中晚期肝癌术后复发率高这一临床痛点，通过先降期干预后联合影像引导精准切除的治疗策略，有望大大降低中晚期肝癌术后复发率。

方法：本研究构建了一种新型 MRI/NIR-II/PAI 多模态诊疗一体化分子探针 IRFEP-FA-DOTA-Gd（IFDG）使其具有显著肝癌细胞靶向性，良好的生物相容性和优良的光热转化性能。

结果：新型靶向分子探针可有效实现对小鼠原位肝癌模型的在体早期精准监测，并且成像信号高峰可维持约 24 h；体内外测试证明其可通过光热效应对原位肝癌细胞进行有效杀伤，通过光热治疗对肝脏部位肿瘤组织干预降期之后，利用探针所具备的 NIR-II/MRI 可有效实现术中实时导引的肿瘤切除，从而达到对肝癌原位病灶彻底切除的治疗效果，并且术后复发程度远小于其他对照组。

结论：本研究所制备的多功能探针及其协同治疗策略可有效降低肝癌术后转移复发率，有望为肝癌的诊疗提供一种全新的策略。

OR-021

磁共振 T2 对比剂 Fe3O4@Cys 的制备及新西兰兔活体成像研究

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目的： 探索反应时间、底物浓度对 Fe3O4 纳米颗粒的影响。制备一种结晶性高、粒径均匀且具有超顺磁性的 Fe3O4 纳米颗粒,使其经半胱氨酸表面修饰后能够稳定分散于水相，并通过 3.0T MR 成像系统经新西兰兔测试其成像性能。方法：采用溶剂热法，通过改变反应时间和底物浓度，制备出不同的 Fe3O4 纳米颗粒。采用 X 射线衍射仪 (X-ray Powder diffractometer，XRD) 对样品进行表征并分析其结晶性，经扫描电子显微镜(scanning electron microscope, SEM)测试其形貌及粒径，选择结晶性较高且粒径均匀的样品进行半胱氨酸（cysteine，Cys）表面修饰，经 ZETA 电位纳米粒度分析仪测试 Fe3O4@Cys 的表面电位及水动力学直径，经震动样品磁强计（vibrating-sample-magnetometer，VSM）等对其进行磁性能测试。使用 3.0T MR 成像系统，通过观察新西兰兔注射前后不同时间点肾脏皮质、髓质及小肠的信号变化，测试其成像性能。结果： 当六水合三氯化铁的用量选择 0.325 g，200℃温度下反应 8h 所制备的 Fe3O4 纳米颗粒结晶性高、粒径均匀，平均粒径约 57.2 nm，经半胱氨酸表面修饰后平均水动力学直径约 201 nm，能够稳定分散于水相，表现出超顺磁性。在磁共振活体成像中具有明显的阴性对比增强效果。结论：反应时间、底物浓度对 Fe3O4 纳米颗粒的结晶性及粒径有影响。制备的 Fe3O4@Cys 纳米颗粒具有超顺磁性，可作为 T2 对比剂用于多种实验和基础研究。

OR-022

多功能纳米脂质体靶向巨噬细胞对动脉粥样硬化不稳定斑块的诊治一体化实验研究

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目的：不稳定动脉粥样硬化斑块破裂造成的心脑血管疾病是全球死亡的主要原因，而 M1 型巨噬细胞向 M2 型的极化可能会使不稳定斑块性质变稳定。我们构建共载 125I-ION 和姜黄素的纳米粒脂质体（9-CCN(125I-ION/Cur)-LNPs），通过单光子发射断层扫描（SPECT）和磁共振成像（MRI）联合的多模态成像手段，将姜黄素靶向输送至动脉粥样硬化斑块，达到诊治一体化目的。

材料与方法：首先，制备 9-CCN(125I-ION/Cur)-LNPs，并检测铁和姜黄素的包封率、载药率以及该纳米脂质体的物理稳定性、放射化学稳定性和弛豫时间。其次，对该纳米脂质体进行体外评估，检测分析 9-CCN(125I-ION/Cur)-LNPs 在巨噬细胞中的摄取情况，并分离兔主动脉粥样硬化斑块中的巨噬细胞。进而，建立新西兰大白兔的动脉粥硬化动物模型，在注射前及每 10 天注射靶向纳米粒脂质体后，分别在注射后 6h 及 36h 进行体内 SPECT 和 MRI 扫描，评估斑块情况。最后，离体兔主动脉，进行病理切片、染色，分析斑块的病理学特征。

结果：透射电镜显示其粒度均一、超顺磁性好、放射化学纯度为 97.2%，且在体内循环中较为稳定。体外摄取研究发现，姜黄素和核素放射性均在 RAW264.7 细胞中摄取较高，而 MRI 图中 ION 的摄取在两种细胞中几乎相同，并且体外实验表明 9-CCN(125I-ION/Cur)-LNP 和姜黄素可促进巨噬细胞极化为 M2 表型。此外，体内实验表明，9-CCN(125I-ION/Cur)-LNPs 可以特异性地与 AS 斑

块中的促炎 M1 型巨噬细胞结合，并将 125I-ION 和姜黄素传递到巨噬细胞中（图 1）。由于 M1 向 M2 极化，不稳定的 AS 斑块变得稳定，导致纳米脂质体吸收显著减少，SPECT/CT 核素摄取下降，T2WI 成像信号减低。

结论：9-CCN(125I-ION/Cur)-LNPs 实现了同时检测和改善 AS 斑块易损性，核医学和磁共振联合成像的方式可精准检测斑块并评估疗效，实现 AS 斑块的诊治一体化。

壁报交流

P0-001

扩散张量成像非侵入性评估肌肉减少症大鼠腰椎旁肌细胞外基质重塑

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目的：骨骼肌细胞外基质重塑是肌肉减少症的主要组织病理学改变之一。本研究的目的是探讨基于磁共振的扩散张量成像技术评估肌肉减少症大鼠腰椎旁肌细胞外基质重塑改变的价值。

方法：将 20 只 6 月龄雌性 Sprague-Dawley 大鼠随机分为地塞米松组（DEX）和生理盐水对照组。两组大鼠均接受 3.0T 磁共振成像扫描，包括 Mensa，T2WI 和扩散张量成像序列。苏木精-伊红染色评估肌纤维的大小。天狼星红染色评估竖脊肌细胞外基质的变化。Western blot 评估竖脊肌中 Collagen I，III 和纤连蛋白的表达。皮尔逊相关分析评估 MRI 定量参数与相应组织病理学标志物之间的相关性强度。

结果：影像学结果显示，相比对照组，DEX 组大鼠竖脊肌横截面积和分数各向异性值显著降低（$P<0.05$）。苏木精-伊红染色显示 DEX 组肌纤维大小萎缩以及排列紊乱；天狼星红染色显示 DEX 组的胶原体积分数显著增加（$P<0.05$）。Western blot 结果显示 DEX 组 I 型胶原，III 型胶原和纤维连接蛋白表达显著增加（均为 $P<0.05$）。分数各向异性值与胶原体积分数，胶原蛋白 I，胶原蛋白 III，纤连蛋白之间的相关系数分别为-0.77，-0.94，-0.85，-0.88（均为 $P<0.05$）。

结论：分数各向异性值与病理胶原体积分数，I 型胶原，III 型胶原和纤维连接蛋白的表达密切相关，表明扩散张量成像技术可以准确地无创性评估肌肉减少症竖脊肌细胞外基质重塑的变化，为肌肉减少症的早期诊断提供潜在的影像生物标志物。

P0-002

超小顺磁性氧化铁纳米颗粒作为磁共振对比剂在肝癌动物模型中的应用研究

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目的：基于氧化铁纳米颗粒的磁共振 T1 对比剂的肝癌动物模型显影及体内代谢研究。

方法：合成直径小于 5 nm 的氧化铁纳米颗粒（Fe3O4 NPs），修饰以聚乙二醇（PEG）。选择 3 kg 左右的新西兰长耳兔，麻醉后在 CT 引导下经皮穿刺肝脏并注射 VX2 瘤块，术后注射青霉素抗炎两天，正常喂养 2 周。后采用剂量 0.025 mmol/kg（同临床用对比剂普美显）的 Fe3O4 NPs 作为造影剂，使用 T1WI、T2WI 序列，进行实验兔对比增强磁共振成像（CE-MRI）不同时间点扫描。观察实验兔肝脏瘤块各时间点大小、形态、增强程度以及与周围组织、血管关系等 特征；同时观察肝脏、胆囊、脾脏及膀胱腔信号变化，以了解其代谢情况。所有指标均与临床用磁共振对比剂进行对比。

结果：Fe3O4 NPs 的体外弛豫率较普美高；当采用 Fe3O4 NPs 作为对比剂成像时，迅速出现类似普美显肝胆特异期时图像，对比同为注射对比剂 15 min 后图像，发现 CE-MRA（Fe）成像时的肿瘤-肝脏间信号对比度较 CE-MRA（Ga）成像时高，可以更好的显示肿瘤的边界、形态；同时，对肿

瘤周围血管的显影也较普美显更清晰，且维持成像时间更长；Fe3O4 NPs 的血管对比增强作用可维持 2 小时以上；而普美显进入血管后迅速扩散至血管外，静脉注射 10 min 后其对血管的增强效果已难达到诊断要求；Fe3O4 NPs 由于其水合粒径较大的原因，无法经肾脏直接滤过，在注入体内 4 小时后，膀胱内尿液未见明显对比增强；而 T2WI 图像上肝脏信号明显减低。

结论：Fe3O4 NPs 可作为一种磁共振 T1 对比剂增强肿瘤-肝脏间的信号对比度；由于较长时间滞留于血管腔，可以长时间动态观察肿瘤周围血管的特征；此外，由于其主要由肝细胞、Kupffer 细胞及体内巨噬细胞吞噬、代谢，而不经肾脏代谢，没有现用钆基对比剂的肾毒性及脑沉积风险。综上所述，Fe3O4 NPs 是一种安全、显影效果良好、具有向临床转化巨大潜力的新型磁共振对比剂材料。

PO-003

3D-MATRIX 技术在脑转移瘤检出的临床应用

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目的　探讨 3D-MATRIX 的脑转移瘤检出能力。方法　收集疑似有脑转移瘤的 59 例患者，用 3.0T-MRI 行增强 5mm-

T1FLAIR、增强 1mm-T1FLAIR 与 1mm-MATRIX 序列扫描。经手术或临床随访 3-6 个月证实为脑转移瘤 28 例患者。按照病灶直径分为 3 组（≤3mm、3-10mm、≥10mm），比较三个序列诊断脑转移瘤的检出数目与按病灶直径分组的检出率。结果　（1）28 例患者共 752 个脑转移瘤病灶，增强 5mm-T1FLAIR、增强 1mm-T1FLAIR 和增强 1mm-MATRIX 脑转移瘤的总检出数分别为 604 个、656 个和 752 个，其中直径≤3mm、3-10mm、≥10mm 分别为 258 个、263 个、347 个，291 个、337 个、349 个，55 个、56 个、56 个。（2）增强 5mm-T1FLAIR、增强 1mm-T1FLAIR 和增强 1mm-MATRIX 的检出数目两两比较，p <0.05，差异有统计学意义。（3）三种序列病灶直径≤3mm、3-10mm、≥10mm 的检出率做卡方检验，p >0.05，差异无统计学意义；病灶直径≤3mm、3-10mm、≥10mm 检出率的线性趋势比较，p <0.05，差异有统计学意义。结论　增强 1mm-MATRIX 对序列脑转移瘤检出率高于增强 5mm-T1FLAIR、1mm-T1FLAIR，特别是对直径≤3mm 的脑转移瘤的检出更有优势，推荐临床常规应用。

P0-004

Application of MRI in tracking and evaluating ruicun-labeled mesenchymal stromal cells transplanted in traumatic spinal cord injury of beagles

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Purpose: This study was to investigate whether ruicun (superparamagnetic iron oxide nanoparticle) labeling can be used to quantify the number of MSCs and observe their dynamic migration with multiparameter MRI using an animal model of TSCI.

Materials and methods: Multiparameter MRI was performed. MR parameters, Texas spinal cord injury scale (TSCIS), and histopathological results were used to evaluate the distribution, differentiation, and repairability of the transplanted cells in TSCI.

Results: Group T showed a significant T2 shortening effect but similar repairability, compared to group M. There was no difference in fractional anisotropy (FA) between group M and group T ($P > 0.05$).

Conclusion: Multiparameter MRI tracked the ruicun-labeled MSCs quantitatively and evaluated the repairability dynamically in a TSCI beagle model.

P0-005

外泌体纳米探针 Exo-USIO 及其联合吉西他滨治疗胰腺癌的实验研究

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目的：胰腺癌是一种消化系统的恶性肿瘤，由于其存在乏血供成像、乏氧致化疗耐药等诊疗困境，导致胰腺癌在早期诊断以及中晚期化疗方面并未获得实质性突破。外泌体具有独特的归巢能力，并可作为载体在体内递送内容物；金属纳米酶可作为显像剂对肿瘤进行成像，还具备类酶活性催化过氧化氢（H_2O_2）产生氧气（O_2）及活性氧（ROS）。本研究利用外泌体靶向归巢及载体的特性，将金属纳米酶靶向递送至胰腺癌肿瘤内，对肿瘤精准成像的同时改善其内部乏氧状态。

方法：通过电穿孔形式将具有 T1 加权成像的纳米酶——超小四氧化三铁纳米粒子(USIO NPs)载入至 Panc-02 细胞衍生的外泌体中，构建外泌体纳米探针 Exo-USIO 并进行表征；采用 Western blot 以及荧光显微镜实验研究 Exo-USIO 细胞水平的类酶效能；通过 CCK-8、流式细胞凋亡等实验研究 Exo-USIO 联合吉西他滨（GEM）抑制乏氧 Panc-02 细胞增殖的效果；通过尾静脉注射 Exo-USIO 研究纳米探针对胰腺癌肿瘤靶向 MR 成像的效果；在尾静脉注射 Exo-USIO 的基础上，联合腹腔注射 GEM，研究 Exo-USIO 联合 GEM 的在体治疗效果。

结果：经一系列表征表明成功制备具有良好稳定性、粒径分布峰值约 122.5nm 的外泌体纳米探针 Exo-USIO。体外细胞实验证明，纳米探针有着较强的归巢能力，能够提高 USIO NPs 进入肿瘤细胞的效率，进而提升类酶效能，催化细胞内源性 H_2O_2 产生 O_2，降低乏氧细胞 HIF-1α 蛋白的表达水平。该纳米探针联合应用 GEM 后，两个 Exo-USIO 浓度组的细胞抑制率分别为 47.2%、60.2%，细胞凋亡率分别为 32.99%、41.79%，均高于单纯 USIO NPs 组。在荷瘤小鼠中，纳米探针 Exo-USIO

显示出对肿瘤靶向 MR 成像的能力，并以对机体几乎无毒的方式克服肿瘤缺氧，在联合应用 GEM 后达到良好的治疗效果。

结论：成功制备外泌体纳米探针 Exo-USIO，其具有良好类酶效能改善肿瘤乏氧，从而加强 GEM 的治疗效果。

P0-006

IDEAL IQ 和 BOLD-MRI 定量评估大鼠股四头肌脂肪浸润和血流灌注对肌肉减少症早期诊断的实验研究

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目的：严重的肌肉减少症可导致重度残疾。早期诊断是目前改善肌肉减少症治疗的关键，在临床实践中迫切需要一种高度敏感和可靠的工具来评估早期肌肉减少症的病程。本研究旨在纵向探讨基于 MRI 的脂肪浸润和血流灌注成像在肌肉减少症发展中的早期诊断价值。

材料与方法：将 48 只 SD 大鼠依据地塞米松注射的不同天数（0,2,4,6,8,10 天）随机分为 6 个组。多模态 MRI 扫描大鼠股四头肌以评估肌肉质量；测量大鼠的四肢握力和游泳力竭时间以评估肌肉的力量和功能。HE 染色和油红 O 染色评估大鼠肌纤维的萎缩和脂肪浸润情况。CD31 免疫荧光染色评估股四头肌的毛细血管形成。通过蛋白质印迹检测 VEGF-A 和 MuRF-1 蛋白的表达。皮尔逊相关分析评估 MRI 定量参数与相应组织病理学标志物之间的相关性强度。最后，通过 ROC 曲线分析 MRI 定量参数在肌肉减少症大鼠成模评估的诊断效能及截断值。

结果：相比对照组，基于 MRI 的定量参数 PDFF、R2*和 T2 值在第二天表现出显著统计学差异，早于第 6 天出现统计差异的 MRI-CSA 值和大鼠四肢握力以及第 8 天出现统计差异的游泳力竭时间（以上均为：$p<0.05$）。 MRI-CSA 与 HE-CSA 值（$r=0.67$；$p<0.001$）；ORO 面积与 PDFF（$r=0.67$；$p<0.001$）；MVD（$r=-0.79$；$p<0.001$）和 VEGF-A（$r=-0.73$；$p<0.001$）与 R2*；MuRF-1 与 MRI-CSA（$r=-0.52$；$p<0.001$）之间存在强相关性。用于成模评估的 PDFF、R2*和 T2 值的 AUC 分别为 0.81（CI 95%：0.69-0.93），0.93（CI 95%：0.86-1.00）和 0.98（CI 95%：0.94-1.00）。

结论：MRI 定量参数 PDFF、R2*和 T2 可用于敏感评估肌肉减少症的早期病理变化。当 PDFF 大于 1.25，R2*大于 53.85，T2 大于 33.88 时，可以判断肌肉减少症大鼠模型成功构建。

P0-007

基于动态扩散荧光层析和深度学习的荧光药代动力学参数成像方法

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基于动态扩散荧光层析成像（D-DFT）技术的荧光药代动力学参数成像在肿瘤早期检测、恶性生物学研究和药效评价等领域具有重要应用价值，但目前其成像方法在物理模型的精确性和方法的定量性等方面尚存明显缺陷，导致重建鲁棒性较低。本文研究基于 D-DFT 和深度学习的肿瘤组

织荧光药代动力学参数成像方法，主要包括：将基于目标鼠解剖结构图谱的非均匀组织光子输运模型与基于分室模型的生物组织荧光动力学方法结合，建立更“逼真”的训练和测试模拟数据集；发展一种基于改进 U 型网络的荧光药代动力学参数重建算法，直接建立组织表面光学动态测量数据与药代动力学参数之间的非线性映射关系，突破成像物理模型的复杂性瓶颈；引入一种基于循环一致性生成对抗网络的风格迁移方法弥合模拟数据与实验数据域之间的差异，完成训练数据集的合理扩充。该方法将实现高空间分辨率、高定量精度的药代动力学参数图像重建，可望为在体肿瘤诊断、药效评估提供一种新思路。

PO-008

基于临床、病理、体素内不相干运动(IVIM)定量参数构建列线图预测宫颈癌组织 PD-L1 表达

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目的：探讨基于临床、病理、体素内不相干运动(IVIM)定量参数构建的列线图预测宫颈癌细胞程序性死亡蛋白配体 1（programmed cell death protein ligand,PD-L1）表达，并评估其预测效能。

方法：回顾性纳入 2021 年 1 月至 2022 年 12 月经病理确诊宫颈癌的 128 例初诊患者，按 7:3 比例将其随机分为建模组(90 例)与验证组(38 例)。所有患者均于治疗前行 IVIM 扫描，对其活检或手术标本行 PD-L1 免疫组化染色。收集患者临床、病理资料，在 IVIM 序列上沿肿瘤实体成分最大层面勾画感兴趣区(ROI)，测量纯扩散系数(D)、灌注分数(f)和伪扩散系数(D*)。采用 χ^2 检验、独立样本 t 检验或 Mann-Whitney U 检验评估 PD-L1 表达阳性组与阴性组间各参数的差异；采用 logistic 回归分析确定其独立相关因素，并分别建立临床病理模型及联合模型，通过 ROC 曲线、校准曲线及决策曲线评估模型预测效能及临床效用。

结果：FIGO 分期、病理分级、宫旁浸润、淋巴结转移、D 值是 PD-L1 表达的独立相关因素，以上述独立相关因素建立的联合模型在建模及验证组中的预测效能良好，AUC 分别为 0.887 和 0.845，高于临床病理模型(AUC 分别为 0.756 和 0.749，$P<0.05$)。基于联合模型建立列线图，Hosmer-Lemeshow 检验示联合模型的拟合度良好（$P>0.05$）；进一步决策曲线显示几乎在所有的风险阈概率下，联合模型的人群净获益高于临床病理模型。

结论：基于临床、病理、体素内不相干运动(IVIM)定量参数构建的列线图可直观、量化预测宫颈癌组织 PD-L1 表达，优于临床病理模型，可为宫颈癌免疫治疗及个性化治疗方式的决策提供理论依据。

P0-009

体素内不相干运动(IVIM)定量参数在宫颈癌组织 PD-L1 表达预测中的临床价值

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目的 探讨体素内不相干运动(IVIM)定量参数在宫颈癌细胞程序性死亡蛋白配体 1（programmed cell death protein ligand,PD-L1）表达预测中的临床价值；

方法 前瞻性纳入 2020 年 1 月至 2021 年 12 月经病理确诊宫颈癌的 78 例初诊患者，术前行 IVIM 扫描，对其活检或手术标本行 PD-L1 免疫组化染色。由 2 名放射科医生在 IVIM 序列上沿肿瘤最大层面勾画 ROI，获取其对应纯扩散系数(D)、灌注分数(f)和伪扩散系数(D*)；利用独立样本 t 检验比较各参数在 PD-L1 表达阳性与阴性组间的差异，Spearman 相关性分析各参数与 PD-L1 的相关性。通过 ROC 曲线评估各参数的预测效能。

结果:PD-L1 表达阳性组的 D 值均较阴性组低(0.66±0.12 vs. 0.74±0.11),差异有统计学意义(P <0.05)；两组间 D*和 f 值比较差异均无统计学意义(P >0.05)，但仍表现出阳性组较阴性组低的趋势(11.21±4.6 vs. 12.43±9.83; 0.17±0.10 vs. 0.18±0.10)。进一步相关性分析显示 D 值与 PD-L1 表达呈负相关(r 值为—0.36，P <0.05)，D*和 f 值与 PD-L1 表达无相关性(P >0.05)。D 值预测宫颈癌 PD-L1 表达的预测效能为 0.85(0.73,0.93)，其特异度为 95.72%。

结论 IVIM 参数 D 值能将病灶内纯水分子扩散与微循环灌注分离，更准确反映肿瘤组织内细胞增殖情况及内在特征，特异性较高，可作为预测宫颈癌 PD-L1 表达的无创影像标记物，为宫颈癌免疫治疗的合适病人选择提供依据。

P0-010

Predictive value of adipose tissue metabolism heterogeneity in the aggressiveness of non-small cell lung cancer

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Purpose: To determine the predictive value of adipose tissue metabolism heterogeneity in the aggressiveness of non-small cell lung cancer.

Methods: A total of 67 patients with pathologically confirmed NSCLC were retrospectively enrolled, and the patients were divided into M0 group and M1 group by M stage. All patients underwent ^{18}F-FDG PET/CT examination within 2 weeks before treatment. CT and PET images of the patients were analyzed to measure the maximum diameter of primary tumor lesions and metabolic parameters such as SUVmax, SUVmean, SUVpeak, metabolic tumor volume (MTV) and total lesion glycolysis (TLG). At the same time, 3D slicer software was used to get SUV, area and volume and other parameters of subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) from ^{18}F-FDG PET/CT. V/S ratio, defined as SUVmax of VAT divided

by the SUVmax of SAT, was also obtained for intergroup analysis, and included subgroup analyses by pathological type and BMI level. Finally, the correlation between ^{18}F-FDG PET/CT semiquantitative metabolic parameters of VAT, SAT and primary tumor lesions was performed.

Results: Among the 67 patients, adenocarcinomas was the most common histologic subtype (71.6%). And there were 24 patients with stage M0 and 43 patients with stage M1. VAT SUVmean (P=0.016), VAT SUVmax (P < 0.001) and V/S ratio (P=0.016) in group M1 were higher than those in group M0. But other parameters related to tumor lesions and adipose tissue were not significantly different between these two groups (P≥0.05). In the subgroup analysis, there was signifcant diference in Ki67 (P=0.022) and maximum diameter of primary tumor (P=0.014) between lung squamous cell carcinoma and adenocarcinoma. VAT SUVmean was significantly different between overweight and obese patients (BMI≥24 kg/m^2) and normal BMI patients (18.5-24.9 kg/m^2) (P=0.022), while no significant differences were found for the remaining parameters (P≥0.05). Further, we demonstrate that the VAT SUVmean was positively correlated with tumor glucose uptake (r=0.401, P< 0.001).

Conclusion: In patients with distant metastasis, VAT SUV and V/S ratio were signifcantly higher than those without distant metastasis, and VAT SUVmean was positively correlated with FDG uptake in primary tumor lesions. These suggest that visceral adipose glucose uptake may serve as a potential biomarker of tumor aggressiveness and predict distant metastasis in patients with NSCLC.

P0-011

脂肪代谢异质性对非小细胞肺癌侵袭性的预测价值

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目的：探究脂肪代谢异质性对非小细胞肺癌侵袭性的预测价值。

方法： 回顾性收集经病理证实的非小细胞肺癌患者 67 例，按 M 分期分为 M0 组和 M1 组。所有患者均于治疗前 2 周内行 ^{18}F-FDG PET/CT 检查。分析患者的 CT 和 PET 图像，测量原发肿瘤最大直径及代谢参数，如 SUVmax、SUVmean、SUVpeak、肿瘤代谢体积(MTV)和糖酵解总量(TLG)。同时利用 3D slicer 软件从 ^{18}F-FDG PET/CT 上获取皮下脂肪组织(SAT)和内脏脂肪组织(VAT)的 SUV、面积、体积、V/S 值等参数进行分析，并按病理类型及 BMI 水平进行亚组分析。最后，进行 VAT、SAT 的 18F-FDG PET/CT 半定量代谢参数与原发肿瘤病变的相关性分析。

结果： 67 例患者中，腺癌是最常见的组织学亚型(71.6%)，M0 期 24 例，M1 期 43 例。M1 组的 VAT SUVmean (P=0.016)、VAT SUVmax (P<0.001)和 V/S 值(P=0.016)均高于 M0 组，而与肿瘤病变及脂肪组织相关的其他参数两组间差异无统计学意义(P≥0.05)。亚组分析中，肺鳞癌和肺腺癌的 Ki67 (P=0.022)和原发肿瘤最大直径(P=0.014)差异有统计学意义。超重和肥胖患者(BMI≥24 kg/m2)与正常 BMI 患者(18.5 ~ 24.9 kg/m2)的 VAT SUVmean 差异有统计学意义(P=0.022)，其余参数差异均无统计学意义(P≥0.05)。此外，我们证明 VAT SUVmean 与肿瘤葡萄糖摄取呈正相关(r=0.401，P<0.001)。

结论： 在有远处转移的患者中，VAT SUV 和 V/S 值明显高于无远处转移的患者，且 VAT SUVmean 与原发肿瘤病变中 FDG 摄取呈正相关。这表明内脏脂肪糖代谢异质性可能作为非小细胞肺癌患者侵袭性的潜在生物标志物，辅助预测远处转移。

PO-012

基于 18F-FDG PET/CT 改良腹膜癌指数预测腹膜假性粘液瘤患者病理分型与无进展生存期相关性研究

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目的：本研究拟通过与 CT-PCI 及 SUVmax 相比较，探究 18F-氟代脱氧葡萄糖（18F-FDG ）PET/CT 改良腹膜癌指数（PET-PCI）对 PMP 患者病理分型、无进展生存期的预测价值。

方法：本研究共纳入 30 例治疗前行 18F-FDG PET/CT 检查，术后经病理证实为 PMP 的患者。评分方法为依照腹膜癌指数（PCI）分区将腹盆部分为 13 个区域，分别计算每个区域 PMP 病灶的 18F-FDG 最大摄取值，通过与纵隔血池、肝脏血池比较进行 PET-PCI 评分，为分别计算 13 个区域内肿瘤病灶最大长径并与 0.5cm、5cm 比较进行 CT-PCI 评分，每个区域评分等级为 0-3 分。

结果：t 检验结果显示，高级别 PMP 患者的 PET-PCI、CT-PCI、SUVmax 显著高于低级别组。Kaplan-Meier 分析显示 PET-PCI（P＜0.001）、CT-PCI（P=0.003）、SUVmax（P=0.005）均与 PMP 患者 PFS 具有显著相关性。单因素 COX 分析中，CEA、CA125 与病理分级为对 PFS 有意义的预后因素，CA19-9 与 PFS 相关性无统计学意义。多因素 COX 分析结果显示，PET-PCI（P=0.005）、SVUmax（p=0.035）是 PMP 患者预后的独立风险因素，而包括 CT-PCI 在内的其他因素与 PFS 相关性不显著。

结论：PET-PCI 有助于术前预测 PMP 的组织病理学特征，PET-PCI=18.5 是诊断的最佳阈值。PET-PCI 和 SUVmax 对预测 PMP 的复发有一定的价值，与 SUVmax 相比，PET-PCI 对无进展生存期的预测更有意义。临床资料如 CEA、CA125 及病理分级也有对复发预测有辅助作用。PET-PCI 作为整合了肿瘤的代谢活动性和 PMP 的累及范围的分子影像学量化指标，有望作为评估 PMP 患者肿瘤负荷的一个新标准，从而对临床治疗方案制定起指导作用。

PO-013

弥漫性中线胶质瘤 H3K27 变异型的影像特征

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【摘要】 目的　通过分析脑弥漫性中线胶质瘤 H3K27 变异型的 CT 和 MRI 影像表现，总结分析其影像学特征，提高对本病的认识。方法　回顾性分析 89 例经手术病理诊断为脑弥漫性中线胶质瘤伴 H3K27 变异型患者的临床和影像学资料。结果　32 例（36.0%）位于丘脑，36 例（40.4%）位于脑干，其余位于脊髓、松果体、三脑室、四脑室、桥臂、小脑、基底节区；66 例（74.2%）形态规则，边界较清；75 例（91.5%）无或轻度瘤周水肿。 肿瘤实性部分 CT 平扫呈等低-稍高密度，T1WI 呈等-稍低信号，T2WI 呈等-稍高或高信号；29 例（32.6%）伴不同程度囊变或坏死，6 例伴出血，7 例伴点状或边缘线样钙化。46 例行 DWI 检查，28 例（60.9%）无或轻度受限，18 例（39.1%）局部明显受限；30 例行 MRS 检查，28 例（93.3%）呈高代谢改变。86 例行 MRI 增强，50 例（58.1%）呈局部花环状高强化，22 例（25.6%）为整体轻度/无强化，12 例（14.0%）呈局部斑片或结节状明显高强化，2 例为整体不均匀明显强化。肿瘤易包绕邻近血管，“基底动脉包绕征”最常见（18 例）；29 例（32.6%）可见“增粗血管进入征”；脑干病灶

中 10 例（27.8%）可见“虎纹征”。结论　脑弥漫性中线胶质瘤 H3K27M 变异型具有一定的影像学特征，有助于术前准确诊断。

PO-014

PET/MRI-informed brain age matrices in Alzheimer’s disease: a systematic review of the literature

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Objectives: The state-of-the-art concept of brain age and brain-predicted age difference (brain-PAD), indicating the brain's accelerated ageing pattern, has been increasingly used as a phenotype in age-related neurodegenerative diseases, especially Alzheimer’s disease (AD). The availability of methods for integrating magnetic resonance imaging (MRI) and positron emission tomography (PET) data has enabled the practical potential of combined anatomical and molecular imaging to be explored. The present systematic review summarizes the diagnostic information provided by PET/MRI in AD patients.

Methods: A literature search was conducted in three different databases. The terms used were “brain age” or “brain-PAD” AND “Alzheimer’s disease” or “Alzheimer’s disease” AND “PET/MRI” or “PET MRI” or “PET-MRI” or “positron emission tomography/magnetic resonance imaging.” All relevant records identified were combined, and the full texts were retrieved. Reports were excluded if (1) they did not consider PET/MRI; or (2) the raw data were not enough to enable the completion of a 2 × 2 contingency table.

Results: The majority of PET studies observed significant metabolic reduction in temporal cortex and hippocampus in AD patients. Structural MRI studies found AD patients had gray matter volume reduction in frontal cortex preferentially, but also in other regions, such including parietal, temporal, and insular gray matter.

Conclusions: In this review, we discuss the application of PET/MRI in the course of AD and summarized region-specific imaging features that closely related to brain age prediction. Combined with MRI, PET will provide a great opportunity to precisely visualize AD from diverse perspectives by using radiolabeled agents and high-resolution morphometric features involved in various pathophysiological processes. PET and MRI imaging techniques help to explore the pathomechanisms of AD comprehensively and find out the most appropriate clinical biomarker in each AD phase, leading to a precise evaluation of brain age and related changes in the course of AD.

PO-015

An antioxidative nanomotor for thrombosis prevention safely

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Maintenance of the balance between antioxidative and reactive oxygen species (ROS) is a basic biological process, excess production of ROS leading to endothelial cell apoptosis and platelet activation, promoting thrombus formation ultimately. Thus, antioxidant has shown great promise in thrombosis prevention. Herein, we report an antioxidant nanomotor, MDPC, which consists of melanin and catalase with further surface modification of polyethylene glycol. Utilization of the interplay between enzyme-catalysis-induced positive chemotaxis, we find that the MDPC specifically converge to injured endothelial cells and activated platelets, and is capable of ROS depletion. Besides that, capitalizing on the reducing properties of melanin, the MDPC mediates the reduction process from trivalent to divalent iron and simultaneously promote the production of disulfide bonds. Our data demonstrate that MDPC exhibit the potent of antioxidative capability in endothelial dysfunction and platelet activation, and suggesting a promising mechanism application for thrombus prevention.

PO-016

磁共振质子密度脂肪分数成像在前列腺癌风险分层中的应用研究

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摘要

目的：基于磁共振质子密度成像获取前列腺癌内脂肪分数，并收集临床及磁共振常规特征，通过多因素 logistics 回归，获得高风险前列腺癌的危险因素。

方法：收集 143 例前列腺增生和 191 例经病理证实的前列腺癌患者的临床资料。所有前列腺癌患者均行机器人辅助前列腺根治切除术或磁共振超声靶向融合穿刺，并进行病理风险分层，其中低风险组（Gleason 评分≤3+4）63 例，高风险组（Gleason 评分≥4+3）128 例。所有患者均接受 3.0T MRI 检查，并统计与前列腺癌相关的临床危险因素。通过多元逻辑回归分析确定能够对前列腺癌风险分层独立的危险因素，建立前列腺癌风险分层预测模型，并进行受试者工作特征（ROC）曲线分析，建立列线图用于可视化分析。

结果：研究显示，前列腺增生组和前列腺癌组在 PV、PSA、全腺体 FF、PPFT 和 SFT 之间差异有统计学意义（$p<0.05$）。前列腺癌低风险组和高风险组在患者 BMI、PV、PSA、肿瘤 ADC 值、标准 T2 信号强度、PI-RADS 评分、病灶脂肪分数和 PPFT 之间差异有统计学意义（$p<0.05$）。GS 和 FF（$\rho=0.6$，$p<0.001$）、PSA（$\rho=0.432$，$p<0.001$）、ADC 值（$\rho=-0.379$，$p<0.001$）以及 PIRADS 评分（$\rho=0.366$，$p<0.001$）呈现显著相关。通过多元 Logistic 回归分析显示，脂肪分数的增加、PIRASD 评分 5 分以及 ADC 值和前列腺体积的减少是高风险前列腺癌的独立预测因子(p=0.000、0.04、0.03 和 0.032)。建立前列腺癌风险分层的预测模型，构建 ROC 曲线显示以 0.67 为模型的最佳截断值，区分高风险前列腺癌曲线下面积为 0.907，灵敏度 78.1%、特异度为 88.9%。

结论：基于磁共振质子密度成像提取前列腺癌内脂肪分数与前列腺癌 Gleason 评分存在显著相关性，是高风险前列腺癌的独立预测因素。

PO-017

The imbalances of ACC GABA/Glx levels in PDM patients may be the mechanism mediating depressive symptoms and pain catastrophe

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Background: The central nervous system (CNS) mechanisms leading to poorer mode and pain sensitization remain totally unclear in primary dysmenorrhea (PDM). The anterior cingulate cortex (ACC) is particularly important for pain unpleasantness with negative mood. Neuroimaging studies have confirmed the structural and functional disruption of pain-related brain networks in PDM patients. Dysfunction of the GABAergic/glutamatergic pathways have been implicated in several chronic pain disorders. However, the specific levels of gamma-aminobutyric acid (GABA) and glutamate/glutamine (Glx) neurotransmitter in the ACC and their relationships with the clinical characters have not been researched in PDM patients.

Methods: Using the MEGA-PRESS sequence and a 3-Tesla MRI (Philips Healthcare, Best, Netherlands), we obtained ACC metabolite concentrations from patients with PDM (n=41) and age- and education-matched healthy controls (HCs) (n=39) in menstruation and periovulatory phases. The GABA+ and Glx levels in the ACC were compared between groups and between two phases in each group, respectively. The GABA and Glx levels in the patient group were correlated with clinical characters.

Results: Compared to HCs, PDMs showed significantly higher Glx levels (Cr referencing; Water referencing; CSF-corrected) and mildly higher GABA+ level (not significantly) in the ACC in menstruation phase. PDMs had the same tread in menstruation phase, when compared to periovulatory phase. In menstruation phase, the SDS/PCS scores of PDM patients had a positive correlation with GABA+ levels (Cr referencing/Cr referencing; Water referencing), respectively.

Conclusion: The imbalances of ACC-GABA/Glx levels in PDM patients in menstruation phase may be the mechanism mediating depressive symptoms and pain catastrophe.

P0-018

Machine learning and the prediction of cerebral ventricular changes in fetuses with ventriculomegaly postnatally: a fetal MRI study

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Background:

It's unclear whether the occipital white matter (WM) radiomics of fetuses with ventriculomegaly (FVs) have changed and can be used to predict postnatal changes in the dilated lateral ventricle.

Purpose:

To evaluate the intracranial structures and occipital WM T2WI radiomics features in healthy fetuses and FVs and to predict the lateral ventricle changes of FVs postnatally based on machine learning.

Materials and Methods:

T2-weighted 1.5-T single-shot fast-spin echo MRI was performed in 52 normal fetuses (NFs) and 95 FVs prospectively in a single center from Jan. 2014 to Aug. 2021 and followed up on the abnormal lateral ventricle changes after birth. Clinical information, intracranial traditional structures, bilateral occipital WM T2WI ROI in NFs, and occipital WM T2WI ROI on the abnormal side (s) in FVs were all gathered and compared. The traditional model, radiomics model, and combined model were established to predict the lateral ventricle changes of FVs postnatally by Random Forest (RF), GaussianNB, and Decision Tree (DT) algorithms, respectively. Receiver operating characteristic curve (ROC) analysis, calibration curve, and decision curve analysis (DCA) were used to validate the predictive performance.

Results:

There were 7 fetuses with postnatal neurodevelopmental delay and 4 fetuses with genetic defects in the FV-stable group, with significant differences between groups. Among the traditional data, there were no significant differences between the FV-resolved and FV-stable groups ($p>0.05$), while significant differences between the NFs and FVs ($p<0.05$), excepting the occipital WM/CSF T2WI SNR ($p>0.05$). The occipital WM T2WI radiomics of FVs differed significantly from those of NFs. Based on the occipital WM T2WI radiomics on the abnormal sides of FVs, it was effective at differentiating NFs from FVs by the three algorithms, with AUC ranging from 0.93 to 1 and 0.79 to 0.94 for the training and validation set. There were some differences in the occipital WM T2WI radiomics between FV-resolved and FV-stable groups. With AUC ranging from 0.86 to 0.97 for the training set and 0.62 to 0.76 for the validation set, the radiomics model based on the same three algorithms may predict lateral ventricle changes in FVs. The combined model predicted lateral ventricle changes much better. The DCA revealed that the combined and radiomics models provided nearly identical clinical benefits.

Conclusion:

Our findings suggest that the occipital white matter on the dilated sides of the FVs may play a key role in the progression of ventriculomegaly, as evidenced by significant T2WI radiomics characteristics associated with changing ventriculomegaly trends.

PO-019

Multiple treatment modes combined with nanotechnology induce pyroptosis to anti-tumor immunity

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Pyroptosis as a new form of programmed death. It is manifested as the caspase cleavage of gasdermin family proteins triggers the cells to expand until the cell membrane ruptures, resulting in the release of cell contents and causing a strong inflammatory response. With the development of multidisciplinary joint diagnosis and treatment, the use of nanotechnology to induce pyroptosis has been a hot topic in the field of tumor therapy. Studies have shown that nanotechnology combined with tumor therapy has a positive effect on promoting anti-tumor immune response. It can be seen that there is an inseparable relationship between pyroptosis and anti-tumor immunity. The research on anti-tumor immunity based on nanotechnology in the mechanism of pyroptosis is deepening. New nanotechnology or nanomaterials can be applied to photodynamic therapy, photothermal therapy, chemotherapy, mitochondrial targeted therapy, nano-catalytic therapy, sonodynamic therapy and other tumor treatment methods to activate different pathways of pyroptosis, which provides ideas for tumor treatment.

Nanomaterials synergistic tumor therapy can induce pyroptosis to trigger anti-tumor immunity. Photodynamic therapy is an optical therapy in which a photosensitizer absorbs an appropriate wavelength under a laser to produce a photochemical reaction to destroy tumor cells. As an intermediate of photodynamic therapy, photosensitizer combines with nanomaterials and produces biotoxic singlet oxygen to kill tumor cells after light activation. In the tumor treatment strategy, nanocatalytic therapy is mainly to stimulate the chemical catalytic reaction of nanoparticles in the body to produce oxidative stress in the tumor. Nanosystem can regulate glucose metabolism to cut off the supply of glucose, which can better induce pyroptosis. Sonodynamic therapy is a new type of non-invasive treatment following traditional therapy and photodynamic therapy. Among them, sonosensitizers synthesized by nanomedicines can shape US-responsive agents to enhance specific sonodynamic effects, such as sonoluminescence-mediated anti-cancer effects. In recent years, mitochondria have attracted much attention as a potential target for anti-tumor immunotherapy. Using nanotechnology to target mitochondria to induce cell death is a method for treating tumors. The sharp increase of Ca^{2+} in the cytoplasm can lead to mitochondrial damage and irreversible cell death. In addition, a variety of chemotherapeutic drugs have been shown to induce pyroptosis of tumor cells. Nanomaterials loaded with chemotherapeutic drugs to form drug delivery systems can

improve the effect of anti-tumor immunotherapy. This nanopreparation can inhibit DNA synthesis, induce cell death and increase the killing activity of T cells. In photothermal therapy, the photothermal materials so far include noble metal nanoparticles with high photothermal conversion efficiency and high unit price, carbon materials with large photothermal conversion area, some metal and nonmetal compounds and organic dye substances. Using nanotechnology to design photothermal materials with good water solubility, strong biosafety, high photothermal conversion efficiency and reduced thermal damage to normal tissues can effectively induce pyroptosis and improve the efficiency of tumor targeted therapy. Photothermal therapy combined with nano-preparation at lower treatment temperature can effectively reduce the thermal damage of surrounding tissues, which is of great significance for future clinical transformation. In addition, multimodal combination therapy can more thoroughly remove tumor cells. For example, photothermal therapy has a good short-term effect on tumors, while photodynamic therapy lasts longer. Photodynamic therapy and photothermal therapy synergistic therapy can complement each other and solve the defects of both. In the existing anti-cancer strategies, whether through single-mode methods such as photodynamic therapy, chemotherapy, nano-catalytic therapy, or even combined with multimodal therapy, these treatment strategies can change the redox balance and acid-base balance inside and outside the tumor to achieve effective inhibition of tumor growth and metastasis. With the increasing value of medical-industrial intersection, it is particularly urgent to find a precise targeted tumor treatment strategy under the promotion of intelligent medical treatment. With the development of precision medicine, it is necessary for us to think and explore the appropriate use of nano-preparations to regulate the tumor microenvironment to achieve positive application value.

PO-020

Fe-mediated self-assembled nanodrug for tumor microenvironment activated synergistic ferroptosis-based-chemodynamic/ chemo therapy and magnetic resonance imaging

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Introduction: Due to the low drug concentration, glutathione (GSH)-based oxidative stress regulating system in target tissues, and its serious side effects, doxorubicin (DOX) usually shows a suboptimal therapeutic effect in clinical practice. The synergistical combination of DOX-based chemotherapy with iron ions based chemodynamic therapy (CDT), sensitization of cancer cells by GSH depletion, and responsive targeted delivery of DOX have been regarded as a potential efficient strategy to improve the therapeutic efficacy.

Objectives: To develop an iron-based poly(lipoic acid) nanomaterial DOX@Fe3+-LA (DOX@FL) which can optimize the cancer therapeutic effect by achieving targeted

magnetic resonance imaging (MRI), drug targeted delivery and tumor microenvironment (TME) activated synergistic ferroptosis-based-CDT/ chemotherapy.

Methods: Benefiting from the strong lipoic acid-Fe3+ coordination, Fe3+ firstly efficiently chelated with DOX, and then mediated the disulfide open-ring polymerization and self-assembly behavior of lipoic acid, synthesizing the proposed DOX@FL nanodrug with a one-pot method. After comprehensive characterization, targeted MRI and TME activated synergistic ferroptosis-based-CDT/ chemotherapy based on DOX@FL nanodrug were explored in vitro and in vivo.

Results: DOX@FL nanodrug with spherical, uniformly distributed morphology and high loading of DOX and Fe was successfully synthesized. Under TME, the nanodrug could synchronously release DOX and Fe, and then induce ·OH generation and intracellular GSH depletion efficiently. After incubated with cancer cells in vitro and administrated in vivo, DOX@FL nanodrug both showed a multimodality synergistic therapeutic effect. In addition, the DOX@FL nanodrug showed pH- and GSH-responsive MRI due to the paramagnetism of Fe3+, suggesting DOX@FL NPs be a good TME-responsive MRI contrast agent in vitro and in vivo.

Conclusion: The developed DOX@FL could synergistically exert DOX-based chemotherapy, iron ions-based CDT, sensitization of cancer cells by GSH depletion, drug targeted delivery and targeted MR imaging, and finally optimize cancer theranostics.

PO-021

A Self-Cascaded Chemo-Photodynamic Prodrug for Fluorescent Imaging-Guided Immunotherapy of Triple-Negative Breast Cancer

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Despite the success of immune checkpoint blockade (ICB) therapy in cancer management, ICB-based immunotherapy of triple-negative breast cancer (TNBC) still suffers from immunosuppressive tumor microenvironment (ITM). To break through the bottleneck of TNBC immunotherapy, a self-cascaded unimolecular prodrug consisting of an acidic pH-activatable doxorubicin and an aggregation-induced emission luminogen (AIEgen) photosensitizer coupled to a caspase-3-responsive peptide was engineered. The generated prodrug, could not only release doxorubicin initiatively in acidic tumor microenvironment, but also activate apoptosis-related caspase-3. The activated caspase-3 could in turn trigger release and in situ aggregation of photosensitizers. Importantly, the unimolecular prodrug exhibits a renal clearance pathway similar to small molecules in vivo, while the aggregated AIEgens prolong tumor retention for long-term fluorescence imaging and repeatable photodynamic therapy (PDT) by only one single-dose injection. Furthermore, the tumor-detained PDT boosts both immunogenic cell death of TNBC cells and maturation of dendritic cells. Finally, the combination of repeatable PDT with ICB therapy further promotes the proliferation and intratumoral infiltration of cytotoxic T lymphocytes, and effectively suppresses

tumor growth and pulmonary metastasis. This prodrug is a proof-of-concept that confirms the first self-cascaded chemo-PDT strategy to reverse the ITM and boost the ICB-mediated TNBC immunotherapy.

PO-022

新型纳米材料联合多种疗法诱导细胞焦亡

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随着多学科的联合诊疗的发展，在肿瘤治疗领域的研究中利用纳米技术来诱导细胞焦亡一直是备受关注的热点。常规的单一免疫治疗在实体肿瘤治疗的效果其实并不理想，纳米材料联合肿瘤治疗疗法在癌症治疗领域有较好的发展前景。通过构建精准功能化的纳米制剂来应对复杂的肿瘤微环境和特殊的肿瘤疾病，为有效诱导细胞焦亡治疗肿瘤提供了新的思路。目前，新型肿瘤免疫疗法主要的抗癌策略是通过多种治疗方法诱导肿瘤细胞死亡。为了实现癌症的早发现、早诊断和早治疗，利用多种肿瘤免疫疗法协同新型的纳米技术和纳米材料能够有效地抑制肿瘤生长和转移，提高肿瘤治愈率。基于现阶段治疗策略中，通过光敏剂制备新型的纳米材料在激光下吸收适当的波长以产生光化学反应杀伤肿瘤的效果，实现光动力治疗。在化学或物理因素的作用下，纳米催化疗法可以激发体内的纳米颗粒发生化学催化反应，在瘤内产生氧化应激的作用。通过纳米材料激活细胞焦亡的分子途径来提高 ROS 水平，能够有效切割 GSDMD 蛋白导致细胞焦亡。声动力疗法是继传统疗法、光动力疗法的一种非侵入性的癌症治疗方法，通过非热超声激活的声学激活剂将癌细胞裂解到组织深处，从而杀死癌细胞，其中，纳米药物合成的声敏剂起着关键作用，它提供了声动力抗癌方法。另外，线粒体靶向治疗是利用纳米技术靶向线粒体诱导细胞死亡的一种治疗方法。可以改变线粒体内外膜的通透性，选择释放细胞色素 C 等内容物到细胞质内来启动细胞死亡。不仅可以设计多功能的纳米材料可以负载化疗药物进入细胞内实现肿瘤治疗。还可以构建出水溶性好、生物安全性强、光热转换效率高且能减少对正常组织热损伤的光热材料，诱导免疫原性细胞死亡，激活全身抗肿瘤免疫反应。迄今为止，纳米技术联合单模式肿瘤治疗能较好地诱导细胞焦亡，有效提高肿瘤抑癌率，提高肿瘤治疗的疗效。除此之外，采用多模式联合疗法来更加彻底清除肿瘤细胞，加强杀伤肿瘤的力度，以减少肿瘤的复发。

PO-023

一种 GBM 靶向 pH 响应性原位 T2 磁共振信号增强的氧化铁纳米复合颗粒

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目的：

胶质母细胞瘤（GBM）呈浸润性生长，目前影像学方法无法精准明确边界，使用磁共振对比剂增强 GBM 病灶处信号有助于精准诊断 GBM。GBM 肿瘤微环境具有弱酸性的特点，利用酸性 pH 响应策略可以有效提升磁共振对比剂在 GBM 病灶处的对比度，从而提高 GBM 的影像诊断精准性。

材料和方法：

基于 PAA（聚丙烯酸）/SPIO（超顺磁性氧化铁）、氯化钙、磷酸氢二钠合成 pH 响应性团聚的纳米复合颗粒 SPIO@CaP（磷酸钙），使用靶向 GBM 的多肽 ^{D}ANG（angiopep-2 多肽的反式镜像异构体）对纳米复合颗粒进行修饰，获得 ^{D}ANG-SPIO@CaP 纳米复合颗粒。细胞层面，采用 CCK-8 试剂盒法评估纳米复合颗粒的细胞毒性，通过铁反应试剂法探究纳米复合颗粒在不同种属细胞内的摄取情况，通过磁共振 T_2 成像评估纳米复合颗粒在不同种属细胞中的摄取成像效果。动物层面，建立 GL261 和 U87-MG 两种不同的小鼠原位 GBM 模型，评估 ^{D}ANG-SPIO@CaP 纳米复合颗粒在小鼠体内的成像效果。最后，对注射纳米复合颗粒的小鼠的主要器官切片进行 HE 染色、对其血清进行生化分析以评估纳米复合颗粒的体内毒性。

结果：

细胞层面的细胞摄取与细胞磁共振 T_2 成像实验中，^{D}ANG-SPIO@CaP 纳米复合颗粒显著提升了肿瘤细胞磁共振 T_2 信号，而对非肿瘤细胞的磁共振 T_2 信号增强不明显。动物层面，^{D}ANG-SPIO@CaP 纳米复合颗粒均能有效地显示两种 GBM 模型的病灶，并且在较长时间内在病灶处观察到 T_2 信号增强。组织切片 HE 染色结果与血清生化分析结果均证明上述纳米复合颗粒具有良好的生物相容性，对细胞以及动物均无明显毒性。

结论：

GBM 靶向 pH 响应性纳米复合颗粒 ^{D}ANG-SPIO@CaP 可以在肿瘤弱酸性环境中发生响应性粒径增大，因而其能在具有弱酸性的 GBM 病灶处发挥更强的磁共振 T_2 增强效果；而且由于其同时具有 GBM 靶向性以及 pH 响应性，^{D}ANG-SPIO@CaP 纳米复合颗粒在具有不同性质的 GBM 中均具备增强的鉴别诊断效能。

P0-024

超小顺磁性氧化铁纳米颗粒作为磁共振新型血池对比剂的动物模型

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摘要

目的：基于氧化铁纳米颗粒的磁共振 T1 造影剂的动物模型显影及体内代谢研究

方法：合成直径约为 3 nm 左右的氧化铁纳米颗粒（Fe3O4 NPs），修饰以聚乙二醇（PEG），形成水合粒径约为 10 nm 的水溶性 Fe3O4 NPs；选择 3 kg 左右的新西兰长耳兔，麻醉后取颈正中切口暴露一侧颈总动脉，采用手术缝线结扎；后采用剂量：0.1 mmol/kg（同临床用造影剂，马根维显）的 Fe3O4 NPs 作为造影剂；使用 3D FLASH 序列，进行实验兔对比增强磁共振血管造影（CE-MRA）不同时间点扫描：观察实验兔各时间点闭塞动脉处显影情况、正常主要血管及其远端细小分支情况；同时采用常规 T1WI 及 T2WI 序列扫描实验兔腹盆腔情况；观察肝脏及膀胱腔信号变化，以了解其代谢情况。所有指标均与临床用磁共振造影剂进行对比。

结果：Fe3O4 NPs 的体外弛豫率较马根维显高；当采用 Fe3O4 NPs 作为造影剂行 CE-MRA 进行血管成像时，可以清楚的显示结扎闭塞部位；主要动静脉及其远端分支也具有极好的显影效果；Fe3O4 NPs 的血管对比增强作用可维持 2 小时以上；而马根维显进入血管后迅速扩散至血管外，5 分钟后其增强效果已难达到诊断要求；Fe3O4 NPs 由于其水合粒径的原因，无法经肾脏滤过，在注入体内 4 小时后，膀胱内尿液未见明显对比增强；而 T2WI 图像上肝脏信号明显减低。

结论：Fe3O4 NPs 可作为一种磁共振血池 T1 造影剂较长时间的保持良好的血管显影效果，增加了检查时间窗，可以获得更多的影像信息；且由于其本身特性其主要由肝脏 Kupffer 细胞及体内巨噬细胞吞噬、代谢，而不由肾脏代谢，没有现用钆基造影剂的肾毒性及脑沉积风险。综上 Fe3O4 NPs，是一种安全、显影效果良好、具有巨大潜力向临床转化的新型磁共振对比剂材料。

PO-025

Biomineralized Ceria Nanoparticles Target the Heart to Improve Diabetic Cardiac Remodeling By Regulating Mitochondrial Oxidative Stress and Decreasing Excessive Mitophagy

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Objective

Diabetic cardiomyopathy is an important factor affecting the prognosis of diabetic patients. Mitochondrial homeostasis imbalance is the standard molecular matrix of metabolic diseases and cardiovascular complications. The specific molecular regulatory mechanisms of mitochondrial oxidative stress and reactive oxygen species production in the pathophysiological state of diabetes are not fully understood. Mitochondrial homeostasis caused by reactive oxygen species may be a critical link of myocardial remodeling in the pathophysiological form of diabetic cardiomyopathy. This study investigated the role of reactive oxygen species and mitochondrial homeostasis in diabetic heart remodeling and novel nanomaterials' effect and potential mechanism.

Methods:

The animal model of type 2 diabetes mellitus was constructed by high-sugar and high-fat diet +STZ, and the relationship between mitochondrial homeostasis imbalance and diabetic myocardial remodeling was investigated by observing the changes in echocardiogram, electrocardiogram parameters, and hemodynamics in diabetic mice, as well as myocardial histopathology, electrophysiology, and molecular biology experiments. The suitable vectors for synthesizing nanomaterials were investigated by RNA-seq analysis and high glucose stimulation of HL-1 cell lines. Synthesis of novel nanomaterials in biomineralization and examination of the biosafety of nanomaterials at the cellular and animal levels, as well as appropriate safe dosages for animal use. By stimulating HL-1 cell lines with high glucose, the therapeutic effects of a high glucose environment on oxidative stress levels, mitochondrial damage of myocardial cells, and novel nanomaterials were initially investigated at the cellular level. Then, in vivo experiments were carried out to evaluate the structural and electrical remodeling of the heart in mice and the effects of treatment with novel nanomaterials on the above cardiac remodeling by body surface electrocardiogram, in

vivo epicardial electrical mapping system, echocardiography in small animals and myocardial histopathology. To explore the potential mechanism of novel nanomaterials to improve cardiac remodeling by protein imprinting technology.

Results:

Echocardiography showed that left ventricular ejection fraction (LVEF) and left ventricular short axis shortening rate (LVFS) were significantly decreased in diabetic mice ($p<0.05$); The thickness of the left ventricular anterior wall and septum reduced the volume of the heart cavity was enlarged considerably, and the ventricular weight was decreased ($p<0.05$). The electrical conduction velocity between myocardial cells in the DM group decreased significantly ($p<0.01$), and the conduction heterogeneity increased significantly. Masson staining of myocardial tissue showed a significant increase in myocardial intercellular fibrosis in the DM group ($p<0.01$). WB showed that the expression of activated AC-MnSOD and α-SMA increased in the diabetic group. In contrast, the expression of mitochondrial dynamics-related proteins OPA1 and DRP1 decreased, and the expression of the protein Pink1/Parkin regulating autophagy clearance of damaged mitochondria was up-regulated. Combined with RNA-seq analysis and protein imprinting experiment, high glucose stimulation significantly increased the TfR gene and protein expression in cardiomyocytes. Using the specific receptor binding properties of TF-TfR and based on the theory of biomineralization, cerium dioxide was combined with Tf to prepare the nanomaterial with good water solubility, stability, high-efficiency nanomaterial enzyme catalytic performance, and excellent biocompatibility--CeO_2@Tf; The nanomaterial combines the specificity of Tf with the antioxidant capacity of cerium dioxide and good biosafety. CeO_2@Tf treatment improved the cardiac function of diabetic mice. Echocardiography showed that both LVEF and LVFS were enhanced. Transmission electron microscopy (TEM) showed decreased autophagosome formation in myocardial tissue after CeO_2@Tf treatment, and Masson staining showed decreased myocardial fibrosis degree after CeO_2@Tf treatment. WB suggested that the expression levels of mitochondrial dynamics and autophagy-related proteins recovered after CeO_2@Tf treatment. Mitochondrial function and stability improved.

Conclusion:

Diabetic disease status/high glucose environment leads to myocardial remodeling and imbalance of mitochondrial homeostasis (mitochondrial fusion, division, mitochondrial autophagy). The biomineralization method synthesized a novel nanomaterial, CeO_2@Tf, which targeted cardiomyocytes mediated by the Tf-TfR receptor and improved cardiac remodeling by regulating mitochondrial homeostasis through the anti-oxidative stress.

P0-026

基于活体比率成像的放疗疗效早评估

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临床现有的肿瘤治疗疗效评估方法往往面临着评估滞后的局限性（>2 周）和一定程度的侵袭性。患者极可能在被确诊为无效治疗前完成了整个治疗方案，从而耽误最佳治疗时间。由此可见实现肿瘤疗效早评估具有重大科学意义。近红外二区（NIR-II）荧光成像因高分辨率，高穿透深度等特点被广泛用于活体深层组织成像。然而，大多数 NIR-II 荧光探针依赖单一通道检测易受外在因素干扰、检测结果误差大，难以实现活性分子在生理和病理状态下的高时空分辨的分布成像和定量检测。激活的 Caspase-3 已被认为是激光、药物和放疗等刺激诱导的癌细胞凋亡的主要介质。发展对激活的 Caspase-3 原位、实时、动态的可视化示踪技术，对其进行精准定量和时空分布的精确监测，有望补充甚至替代临床现有的疗效评估方法。

本课题构建了一种 Caspase-3 响应、具有双通道信号的比率型 NIR-II 荧光探针 DCNP@IR-806，用于对活体内放疗激活的 Caspase-3 进行无创、低信噪比的实时成像和精准定量。肿瘤部位的探针经放疗后，肽链会被激活的 Caspase-3 特异性剪切导致荧光敏化天线 IR-806 脱落。此时，对于一个粒子，其在 980 nm 激光激发下的 1550 nm 处的荧光（FLex980,1550）不变，而在 808 nm 激光激发下的 1550 nm 处的荧光（FLex808,1550）变弱。体内外实验都发现探针的比率信号（FLex980,1550/FLex808,1550）和放疗激活的 Caspase-3 的量在一定范围内呈正相关。随后以放疗后激活产生的 Caspase-3 为桥梁，课题建立了 48 h 内的 NIR-II 比率荧光信号与肿瘤放疗疗效之间的关系。经统计，我们将治疗后 12 h 测得的比率荧光信号划分为三个区间，分别对应无效治疗、有效治疗以及高效治疗。本课题构建的放疗疗效早评估体系，可实时反馈治疗效果，及时调整治疗策略，提高疗效，实现肿瘤个性化、精准化的“按需”治疗，为临床肿瘤放疗疗效早评估提供了一种强有力的方法。

P0-027

基于吲哚-七甲川-喹啉花菁的成纤维细胞活化蛋白靶向近红外荧光探针的设计与合成

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目的：本课题设计并合成了一种成纤维细胞活化蛋白抑制剂（FAPI）-吲哚-七甲川-喹啉花菁近红外荧光探针 FAPI-I-Q-Cy7。花菁染料中磺酸根的引入能够改善探针的光量子产率，其不对称性结构有利于增加分子内电荷转移效应，进而增大染料的 Stokes 位移，从而取得良好的显像效果。连接子中聚乙二醇（PEG）的引入可以优化探针的水溶性和药代动力学性质。探针有望为临床肿瘤早期发现及术中导航提供支持。

方法：以 FAPI 喹啉结构为母核，通过 12 步反应构建模块 A（N3-PEG-哌嗪-N 杂脂肪链-喹啉靶头）；以苯胺、环己酮、2,3,3-三甲基假吲哚、3-(2-甲基喹啉-1-基)丙烷-1-磺酸内盐等为原料，通过 4 步反应，构建模块 B（含有一个吲哚-端炔结构和一个喹啉-磺酸根的结构不对称的 Cy7），然后通过铜（I）催化的炔-叠氮环加成（CuAAC）点击缩合反应将模块 A 和 B 进行接合即

可合成 FAPI-I-Q-Cy7，之后通过半制备型高效液相加以纯化可得探针纯品。后续可以通过理化性质、光学性质以及各种生物学表征手段对目标探针进行评价和根据评价结果指导进一步的结构优化。

结果：目标探针 FAPI-I-Q-Cy7 经纯化完成后纯度大于 98%，借助核磁共振氢谱、核磁共振氟谱以及质谱等表征手段对其进行了结构确证，质谱谱图上可见探针的[(M+H+2Na)/3]$^{+}$峰：481.15。探针的最大紫外吸收波长为 732 nm，最大荧光发射波长为 839 nm。初步实验结果表明探针 FAPI-I-Q-Cy7 适合用于细胞和活体显像实验，更为深入的生物学表征及结构改造正在稳步推进中。

结论：本课题成功设计并合成了一个靶向 FAP 的近红外荧光探针 FAPI-I-Q-Cy7，其最大紫外吸收光谱和荧光发射光谱处于近红外一区波长范围内，适合用于肿瘤学领域的体内外显像研究。

P0-028

“双同弹头”靶向成纤维细胞活化蛋白近红外荧光探针的设计与合成

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目的：本课题设计并合成了一种成纤维细胞活化蛋白抑制剂（FAPI）二聚体-吲哚菁 Cy7 近红外荧光探针。“双同弹头”靶向基团有望增强探针对成纤维细胞活化蛋白（FAP）的靶向性，增加肿瘤部位对探针的摄取，提高显像的靶本比，改善在荷瘤活体中的显像效果。

方法：以 FAPI 喹啉类结构为母核，通过 12 步反应引入 N3-linker（N3-PEG-哌嗪-N 杂脂肪链），构建模块 A（N3-linker-喹啉靶头）；以苯胺、环己酮、2,3,3-三甲基假吲哚等为原料，通过 3 步反应，构建模块 B（含有两个端炔基团的结构对称的吲哚菁 Cy7）；然后通过铜（I）催化的炔-叠氮环加成（CuAAC）点击缩合反应将模块 A 和 B 进行整合，在 Click 反应中通过调整投入 A 和 B 的比例，两倍量 A 与一倍量 B 反应可以主要生成含有“双同弹头”的近红外荧光探针(FAPI)2-Cy7，一倍量 A 与一倍量 B 反应，主要生成“单弹头”的对照探针 FAPI-Cy7。之后从理化性质、光学性质、细胞学实验、活体显像等方面对其进行表征，以此结果反馈对探针结构的改造，以期获得一些药代动力学性质优良，显像靶本比高的双重靶向 FAP 的近红外荧光探针。

结果：目标探针(FAPI)2-Cy7 及对照探针 FAPI-Cy7 经半制备型 HPLC 纯化后纯度均大于 98%，并借助核磁共振谱及质谱等表征手段对其结构进行了确证，质谱谱图可见(FAPI)2-Cy7 的[(M+2H)/2]$^{+}$峰：1067.11，FAPI-Cy7 的质谱谱图可见[(M+3H)/3]$^{+}$峰：454.70。探针的最大紫外吸收波长为 784 nm，最大荧光发射波长为 826 nm。(FAPI)2-Cy7 在高达 3 mM 浓度下对 U87 细胞系仍未显示出明显毒性。

结论：本课题设计并成功合成了“双同弹头”的 FAPI 二聚体-吲哚菁 Cy7 近红外荧光探针(FAPI)2-Cy7，探针的最大紫外吸收和荧光发射光谱落在近红外一区，同时探针具备良好的生物相容性，具备开展深入的细胞学和显像研究的价值。

P0-029

MRI 引导下肿瘤相关巨噬细胞靶向纳米材料用于肝转移瘤免疫治疗

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目的

开发了一种 MRI 引导下的肿瘤巨噬细胞（TAMs）靶向的纳米平台，以克服肝转移瘤的药物耐受、渗透性低等缺点，并提供实时治疗评估反应。

方法

TAMs 靶向的磁性纳米颗粒 NP 是由多巴胺修饰的透明质酸（HA-DA）存在氯喹和亚铁离子的简易一锅法制备的。采用动态光散射粒度仪以及 X 射线衍射仪等检测对 NP 进行表征。采用肝转移小鼠模型，观察 NP 在体内肿瘤增强中的 MRI 效果。然后，评价 NP 的体外和体内的细胞毒性及免疫治疗作用。

结果

我们选择粒径约 69 nm 的 NP 研究肿瘤巨噬细胞靶向的诊疗作用。NP 中的纳米粒子 Fe3+固有的超顺磁性，使其成为 MRI 对比剂的潜力。NP 具有较高的纵向弛豫率（r1），约 145mM-1s-1，使 NP 成为一种高效的对比剂。肝转移瘤小鼠尾静脉注射 NP 行 T1WI，我们发现肝脏区域变暗，而转移灶变得信号增高。注射后 1 小鼠，肝转移灶与周围正常肝组织明显不同，转移灶的对比度噪声比最高。相比之下，在 T1 注射临床使用的肝特异性普美显的小鼠肝转移瘤图像中，转移瘤与周围肝组织的信号接近而无法诊断。在治疗方面，NP 治疗组显示肿瘤明显缩小，在随访期间没有复发，我们猜测氯喹可使 M2 巨噬细胞显著极化为 M1 巨噬细胞，重塑肿瘤微环境，从而具有肿瘤免疫治疗作用。

结论

综上所述，开发了一种采用一锅法高效合成纳米 NP 体系。一种具有优异的 MR 成像的纳米治疗剂。该策略还表明，TAMs 极化治疗联合 PTT 诱导的 ICD 可以显著提高免疫治疗的疗效。因此，本课题将为 MRI 引导下的重塑免疫微环境增效肿瘤治疗研究提供新的策略，具有重要的理论和临床转化价值。

P0-030

近红外二区花菁-蛋白荧光纳米探针用于肿瘤及胃肠道手术导航

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目的：

常规肉眼指导手术操作具有手术并发症及残留病灶的风险，而影像引导下的手术导航技术有助于提高手术的准确性和安全性。第二近红外窗口（NIR-II）荧光成像是术中实时成像的一种重要技术，进一步提高了荧光成像的分辨率与组织穿透深度，降低了背景荧光和光学散射。花菁类染料新吲哚菁绿（IR820）与临床批准使用的吲哚菁绿（ICG）的结构相似，具有良好的荧光稳

定性，通过与白蛋白相互作用可以生成荧光增强发射的花菁-蛋白荧光纳米探针。因此，设计近红外二区花菁-蛋白荧光探针用于肿瘤及胃肠道手术导航对于不同的生物学应用具有重要意义。

方法：

使用 1:2 的摩尔比的 IR820、人血清白蛋白水溶液室温下搅拌一小时，无需提纯得到 IR820-白蛋白复合物。使用紫外分光光度计、荧光光谱仪、NIR-II 荧光成像仪等对材料性能进行表征；使用 MTT 和组织病理切片进行材料毒性研究；NIR-II 荧光成像引导下对小鼠胃肠道梗阻和肿瘤模型进行手术治疗。

结果：

通过在不同给药路径中应用 IR820-白蛋白复合物荧光探针，成功实现了小鼠胃肠道梗阻和肿瘤的 NIR-II 荧光成像手术导航。IR820 与白蛋白之间相互作用强烈，合成的 IR820-白蛋白复合物荧光性能优越，光学稳定性、胶体稳定性和热稳定性良好，同时具有良好的生物相容性。基于口服或静脉给药途径中白蛋白的含量不同，制备的 IR820-白蛋白复合物荧光探针能够实现用于 NIR-II 荧光成像手术导航，使得肿瘤和胃肠道轮廓清晰可见，成功实现肠梗阻解除及肿瘤切除手术。

结论：

基于 IR820 优越的 NIR-II 荧光特性和白蛋白的荧光增敏作用，我们提出了一种适用于 NIR-II 荧光成像和手术导航的不同给药途径方案，包含静脉给药后 IR820-白蛋白复合物的体内自发形成和口服给药途径所需的体外 IR820-白蛋白复合物的预合成，成功完成了胃肠道系统和肿瘤的实时 NIR-II 荧光成像及手术导航。因此，IR820-白蛋白复合物在针对不同疾病的 NIR-II 成像引导手术中显示出广阔的应用前景。

P0-031

新型靶向 alpha 型雌激素受体 18F 标记放射性探针的设计、合成及初步生物学性质评价

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目的：雌激素受体 α（ERα）阳性分型占所有乳腺癌病例的 70%左右。本课题拟基于四氢吡啶并吲哚骨架开发一类新型靶向 ERα 的 ^{18}F 标记放射性分子探针，使 PET 技术运用于乳腺癌的诊疗更具备指导意义。

方法：以 L-色氨酸甲酯盐酸盐为起始原料，依次经历碱化游离氨基，氢化铝锂还原，氨基、羟基的保护，氢气氛围下氢氧化钯/炭催化还原，亲核取代共计 6 步反应来构建(R)-α-甲基吲哚丙胺，(R)-α-甲基吲哚丙胺模块与 4-位长链（链末端为-OTs）取代的苯甲醛模块经由 Pictet-Spengler 反应可以制得含有-OTs 基团的标记前体，利用 ^{18}F-对-OTs 的亲核取代来合成 ^{18}F 标记的放射性探针，之后经纯化和富集可获探针纯品，后续对其进行了理化性质表征和生物学性质评价：测定其脂水分配系数、稳定性、利用细胞摄取和阻断实验探究探针的靶向特异性、考察其药代动力学性质。

结果：合成了 **R1-R4** 共计四个放射性探针，其放化收率在 1-41%之间，放化纯度均大于 99%，logP 在 1.65-2.49 之间，四个放射性探针与磷酸盐缓冲液（pH = 7.4）或小鼠血清在 37 ° C 共孵育至少 4 小时内保持稳定。对其中两个探针进行了初步的生物学表征：探针 **R1** 在 ERα^{+}细胞系 MCF-7 中的摄取可以被对应的非放射性探针强烈阻断，探针 **R2** 在 ERα^{+}细胞系 MCF-7 和 ERα^{-}细胞系 MDA-MB-231 中的摄取也表现出了较为显著的差异性，这些结果初步表明此类探针可特异性靶向 ERα。血液药代动力学结果表明：探针 **R1** 在正常小鼠体内以一级动力学方式消除，分布半衰期约

为 0.96 min，消除半衰期约为 37.3 min，主要在组织中分布。对这些探针更为深入的生物学评价正在进行中。

结论：本课题基于四氢吡啶并吲哚骨架设计并合成了四个靶向 α 型雌激素受体的 ^{18}F 标记放射性探针，对其理化性质进行了表征，并对其中的两个探针进行了初步的生物学评价，此类探针初步显示出较好的靶向特异性和药代动力学行为，有望在动物实验中取得良好的显像效果。

PO-032

甲硫氨酸氨肽酶-2 响应型自组装纳米正电子发射型计算机断层显像/荧光双模态探针的设计与合成

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目的：甲硫氨酸氨肽酶-2（MetAP-2）在多种癌症中均有较高表达，本课题拟设计并合成基于 2-（2′-羟基苯基)-4-(3H)-喹唑啉酮（HPQ）的新型 MetAP-2 响应型自组装纳米正电子发射型计算机断层显像（PET）/荧光双模态探针 Met-HPQ-^{18}F，其经肿瘤细胞中 MetAP-2 酶切激活后生成的 HPQ-^{18}F 可自组装聚集成为纳米颗粒而增加在细胞中的滞留，引起聚集诱导发光（AIE）可用于细胞荧光显像，同时也可用于荷瘤活体的 PET 显像。

方法：目标探针 Met-HPQ-^{18}F 的化学结构由四个模块组成：固态有机荧光团 HPQ、通过三氮唑与 HPQ 连接的 N,N-二甲基氨甲基三氟硼酸盐（$AMBF_2{}^{18}F$）结构、酶特异性识别的甲硫氨酸残基、甲硫氨酸残基和 HPQ 之间的自毁基团。探针的合成方法为：以 2,5-二羟基苯甲酸为原料，经丙酮叉保护、Mitsunobu 反应、二异丁基氢化铝还原、成环构建喹唑啉-4-酮、铜(I)参与的炔与叠氮的 Click 缩合等 10 步反应得到非放射性探针 Met-HPQ-F，最后通过 ^{18}F-^{19}F 同位素交换即可顺利制得探针 Met-HPQ-^{18}F，可用于后续生物学评价。

结果：成功获得了 MetAP-2 响应型自组装纳米 PET/荧光双模态目标探针 Met-HPQ-^{18}F 前体 Met-HPQ-F，经半制备型 HPLC 纯化完成后获得产物 20 mg，纯度达 99%以上，并借助核磁共振谱图及质谱等手段对其结构进行了确证，ESI-MS 谱图中可见$[M+H]^+$峰：906.63。Met-HPQ-F 可用于后续 ^{18}F 标记制备目标探针 Met-HPQ-^{18}F。

结论：本课题设计并成功合成了探针前体 Met-HPQ-F，可用于制备 MetAP-2 响应的自组装纳米 PET/荧光双模态探针 Met-HPQ-^{18}F，该探针可在酶激活后释放出 HPQ-^{18}F 而在肿瘤细胞内发生自组装聚集，不仅可以通过 AIE 用于细胞荧光显像，亦可在荷瘤活体的 PET 显像时获得高靶本比的图像，有望为 MetAP-2 抑制剂的筛选和开发提供一种有前景的工具。

PO-033

高动力学稳定性和 T1 弛豫效能的支化大分子钆基造影剂的制备与磁共振成像应用

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引言：基于支化大分子的造影剂因具有高的动力学稳定性和 T1 弛豫效能而被广泛用于磁共振成像。然而，传统支化大分子造影剂是将小分子造影剂接枝到支化大分子表面，这一制备策

略不仅造成支化大分子骨架浪费，而且 T1 弛豫效能提升有限 。因此，本文拟通过简单的‘A2+B4’ 的聚合方式，一步法制备以大环钆螯合物（DOTA-Gd）为骨架的支化大分子造影剂，其具有更高的动力学稳定性和 T1 弛豫效能。

材料与方法：1）通过‘A2+B4’的聚合方式，并通过调节聚合时间，获得四种分子量和支化程度不断提高的支化大分子（G1、G2、G3 和 G4），随后在 pH 7.4 螯合钆离子，获得相应的钆螯合物（G1-Gd、G2-Gd、G3-Gd 和 G4-Gd）；2）通过偶氮肿 III（ASIII）竞争实验，评估四种支化大分子钆螯合物在 pH 1.5 条件下的动力学稳定性； 3）在 0.5、1.5 和 3.0 T 磁场下评估四种支化大分子造影剂的 T1 弛豫效能，并选择其中动力学稳定和弛豫效能最高的造影剂进行体内磁共振成像评估。

结果与讨论：钆离子可以与 ASIII 结合形成复合物，从而在 660 nm 处出现 一个新的紫外吸收峰，因此可以用于计算钆离子的解离百分比（图 1b）。如图 1c 所示，线性 DTPA-Gd 由于动力学稳定性低，168 h 后钆离子基本解离；而四种支化大分子钆造影剂只有 30%左右的钆离子发生解离。其中具有最高分子量和支化程度的 G4-Gd 的钆解离百分比显著低于 G1-Gd 以及钆布醇（gadobutrol）。另外，四种支化大分子钆造影剂的 T1 弛豫效能显著高于 DOTA-Gd，且随着分子量和支化程度增加，弛豫效能也增大（图 1d）。相比于小分子 DOTA-Gd，G4-Gd 具有更清晰，更长时间的心血管和头部血管成像效果，且可以清晰的分辨出 1000 μm 以下的血管（图 2）。

结论：我们成功制备了具有高动力学稳定性以及 T1 弛豫效能的支化大分子钆造影剂，并具有优异的心血管及头部血管成像效果。

P0-034

一种骨架刚性的 Fe(III)螯合物磁共振造影剂

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目的：

利用 Fe^{3+}制备一款生物安全性高、弛豫增强效果好的小分子磁共振造影剂，有望成为临床钆基造影剂的有效替代品，进而解决使用钆基造影剂引起的生物安全性问题。

方法：

通过弛豫率分析仪（0.5 T）测定 Fe-CDTA 的弛豫率；通过 UV-vis 测定 Fe-CDTA 在不同条件下的动力学稳定性；以 Gd-DTPA 为对照，利用 CCK-8 法测定 Fe-CDTA 的细胞毒性（4T1 细胞）；在正常小鼠和荷瘤小鼠模型进行体内成像实验（3.0 T）和药代动力学分析；利用 ICP-MS 研究注射造影剂 24 小时后小鼠体内残留情况。

结果：

Fe-CDTA 的弛豫率为：r_1 = 1.16 $mmol^{-1}s^{-1}$, r_2 = 1.20 $mmol^{-1}s^{-1}$（0.5 T, 32° C)；在强酸性条件下（HCl = 100 mM)），Fe-CDTA 的 UV-vis 特征吸收在 72 小时内无变化，表明 Fe-CDTA 在上述条件下具有较高的热力学稳定性；在 Zn^{2+}离子竞争实验中（Hepes，pH = 7.4，[Fe] = [Zn] = 100 μM），Fe-CDTA 的 UV-vis 特征吸收在 72 小时内无变化，表明 Fe-CDTA 在上述条件下具有较好的动力学稳定性。CCK-8 实验表明，在 30-500 μM 浓度范围内，Fe-CDTA 与 Gd-DTPA 具有相似的低的细胞毒性。小鼠体内成像结果表明，Fe-CDTA 是典型的细胞外液造影剂，其血药动力学、体内分布和

清除与 Gd-DTPA 相似；在荷瘤鼠成像中（4T1），Fe-CDTA 对病灶的对比增强效果与 Gd-DTPA 相似。注射造影剂 24 小时后，ICP-MS 测量结果表明造影剂在各组织器官中无残留。

结论：

Fe-CDTA 是一款稳定性高、毒性低、体内对比增强效果好、体内无残留的非钆细胞外液磁共振造影剂，是现有临床钆基造影剂潜在的有效替代品。

PO-035

超顺磁性四氧化三铁多功能分子探针的制备及在兔早期小肠缺血的应用研究

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目的　制备 Fe3O4 磁性纳米颗粒（Fe3O4@CA），评估其磁热疗性能；经半胱氨酸表面修饰后（Fe3O4@Cys），应用于评估兔小肠早期急性肠系膜上动脉缺血（AMI）肠壁损伤。

材料与方法 采用共沉淀法合成 Fe3O4@CA。将样品加入半胱氨酸溶液，制得 Fe3O4@Cys。（1）将 Fe3O4@CA 室温下置于磁感应加热装置（AMF）中，用红外热成像仪记录温度。（2）将 30 只新西兰雄性白兔随机分为实验组（n=15）和对照组（n=15）。实验组结扎肠系膜动脉，随后分别于 1、2、3、4、5 h 进行 MR T2-mapping 成像，肠内给药（Fe3O4@Cys）后行 MR T2-mapping 成像，并记录前后 T2 值差值，每个时间点 3 只兔。对照组行假手术。取病理标本进行普鲁士蓝染色，评估小肠肠壁缺血损伤的严重程度和肠壁内分子探针含量变化。各个时间点实验组与对照组数值差异采用独立样本 t 检验，两组各时间点 T2 值差值的组内比较采用单因素方差分析，并用病理组织学进行相关验证。

结果　（1）在 474KHz，电流为 34.7A 的 AMF 中，0.4g/ml 的 Fe3O4@CA 的温度能在 5min 内从 30℃升高到 48℃。（2）实验组 5 个时间点的 T2 值差值均高于对照组，差异有统计学意义。实验组 5 个时间点的 T2 值差值差异有统计学意义（。随着缺血时间的进展，T2 值差值逐渐增大。前 3 h 病理表现以黏膜层、黏膜下层的损伤为主，铁聚积的范围亦为黏膜层与黏膜下层，且铁含量随肠壁损伤程度增加；缺血 4 h 时肠壁损伤到达肌层，此时肌层内出现少量蓝染的铁；缺血 5　h 时黏膜层、黏膜下层细胞崩解，肠壁损伤累及大部肌层，肌层内铁含量进一步增加。

结论　Fe3O4@CA 在特定磁场中升温特性明显，具有良好的磁热治疗应用前景。MRI T2-mapping 定量成像联合 Fe3O4@Cys 分子探针有助于定量评估 AMI 小肠肠壁损伤，对于疾病的分期具有一定的优势。