Translational Ultrasmall Particle Imaging Tools for Molecular Cancer Imaging and Intraoperative Treatment

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Despite recent advances in imaging probe development for biomedicine, the translation of targeted diagnostic platforms remains challenging. Nanomaterials platforms currently under evaluation in oncology clinical trials are largely non-targeted drug delivery vehicles or devices to thermally treat tissue; these are typically not surface modified for targeted detection by clinical imaging tools. New tumor-selective platforms need to satisfy critical safety benchmarks, in addition to assaying targeted interactions with the microenvironment and their effects on biological systems. Coupled with metabolic imaging and analysis tools, such as PET, complete and quantitatively accurate data sets for whole body distributions, targeting kinetics, and clearance profiles of new diagnostic platforms undergoing preclinical testing or transitioning into early-phase clinical trials can be acquired.

In the operating theatre, there is also an urgent need for implementing new image-directed visualization tools that can enhance surgical vision, facilitate minimally invasive surgical procedures, and dramatically alter surgical outcomes of oncological patients. The lack of clear surgical vision impacts the ability of the operating surgeon to accurately and specifically identify the extent of malignancy, microscopic tumor burden, or remnant disease. Collectively, these factors affect therapeutic outcome, prognosis, and treatment management. Newer molecular imaging probe designs coupled with state-of-the-art device technologies, may enhance cancer care, provide real-time imaging guidance, and lead to new, more efficient approaches for early-stage detection and treatment.

Advances in nanotechnology have also fueled a paradigm shift in targeting and safely delivering drugs in conjunction with image-directed approaches. The size, architecture, and chemical composition of particle-based drug delivery vehicles can be fine-tuned to achieve properties optimal for loading and controlled release of therapeutic agents, patient safety/compliance, favorable kinetic profiles, and reducing unwanted side effects. By combining therapeutic particle tracer preparations with quantitative bioimaging approaches, drug delivery, lesion localization, and the extraction of key tumor biologic properties can be achieved for individualizing treatment planning. In turn, dosage regimens needed to achieve therapeutic efficacy might be estimated based on knowledge of drug specific activity and dose, uptake kinetics, and IC₅₀ values.

The ability to flexibly adapt the formulation of clinically-promising drugs to improve their physicochemical and/or biological properties, in combination with metabolic imaging tools, will be important to quantify and establish suitable clinical trial endpoints. Issues relating to solubility, transport, barrier penetration, time-dependent changes in drug uptake, and intratumoral distribution are additional considerations. These properties are often not generally evaluated in the context of drug delivery due to the complexity of the biological systems involved and the inability to serially monitor this process non-invasively in the absence of drug labeling. The future success of molecular medicine will, in part, rest upon our ability to offer improved clinical trial designs addressing the foregoing issues. In conclusion, the adoption of such an approach for image-directed drug delivery in clinical settings will have far-reaching implications for personalizing cancer care in terms of treatment planning, stratification to appropriate trial arms, and response monitoring.