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A REVIEW ON THERANOSTIC ADVANCEMENTS IN COLORECTAL CANCER: INTEGRATING MOLECULAR IMAGING AND NANOTECHNOLOGY FOR PRECISION ONCOLOGY

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ABSTRACT

Colorectal cancer is still among the leading causes of morbidity and mortality globally, thereby creating an urgent need for innovative diagnostic and therapeutic strategies. Theranostics is an integrated approach combining diagnosis and therapy within a single platform; this offers enhanced precision in tumor detection, targeted drug delivery, and treatment monitoring. This review synthesizes literature from 2020 to 2025 to examine key developments in CRC theranostics, including molecular imaging modalities, targeted therapy platforms, and advanced nanotechnology-based systems. PET/CT, PET/MRI, MRI, and optical imaging modalities significantly improve staging, localization, and intraoperative visualization. Accordingly, these nano theranostic platforms, such as gold nanoparticles, liposomes, polymeric nanoparticles, SPIONs, mesoporous silica nanoparticles, and quantum dots, have been shown to contain dual capabilities for imaging enhancement and controlled drug release. Despite this progress, translation into clinical practice remains limited due to challenges pertaining to nanotoxicity, scalability barriers, and

restrictive regulatory status. Future progress requires standardized toxicity testing, advanced molecular imaging integration in clinical trials, and scalable nanoparticle manufacturing. Theranostics heralds a potentially transformative shift toward personalized and image-guided CRC management.

KEYWORDS: Colorectal cancer, Theranostics, Nanoparticles, Molecular imaging, Targeted therapy, PET/MRI, SPIONs.

INTRODUCTION

CRC is one of the most common malignancies in the world, with a high mortality rate despite advances in screening and therapeutic options. The deficiencies of traditional imaging techniques, such as the inability to detect micro metastasis and limited accuracy in assessment of treatment response, emphasize the need for developing more advanced diagnostic modalities. Theranostics integrates diagnostics and therapeutics within one platform that facilitates real-time disease characterization, targeted delivery, and monitoring therapy.

These include radio-theranostics, magneto-theranostics, opto-theranostics, and nano-theranostics, which provide improved tumor detection and controlled therapeutic payload release by means of radiotracers, magnetic nanoparticles, optical probes, and multifunctional nanomaterials. Molecular imaging technologies such as PET, PET/CT, PET/MRI, MRI, fluorescence imaging, and photoacoustic imaging have transformed the management of CRC through enhanced staging, surgical navigation, and personalized treatment planning.

Meanwhile, parallel progress in nanotechnology has yielded polyvalent nanocarriers consisting of gold nanoparticles, liposomes, PLGA nanoparticles, MSNs, dendrimers, carbon nanotubes, and quantum dots. All these systems possess high biocompatibility, tunable surface functionalization, and dual-function capability for both imaging contrast enhancement and therapy delivery. Despite promising progresses, clinical adoptions are still very limited, mainly owing to the toxicity, immunogenicity, long-term safety, and difficulties in large-scale nanoparticle synthesis following GMP criteria.

This review systematically synthesizes recent developments in CRC theranostics, identifies major technological and translational barriers, and discusses the future directions needed to attain clinical integration.

2. Theranostic Modalities in CRC

2.1 Molecular Imaging Platforms

2.1.1 PET, PET/CT, and PET/MRI

PET is indispensable for staging, follow-up of recurrence, and planning treatment in CRC. Combined imaging by PET/CT provides both whole-body metabolic and anatomical information; simultaneously acquired PET/MRI offers lower radiation exposure and superior soft tissue contrast-especially during the staging phase of rectal cancer. PET/MRI shows much promise because it allows for improved delineation of tumor margins and has reduced radiation exposure.

2.1.2 MRI and Advanced Contrast Agents

MRI delivers high-resolution imaging in soft tissues, the cornerstone of rectal cancer management. Advanced contrast agents, including ultra-small and superparamagnetic iron oxide nanoparticles, are reviewed to improve lymph-node metastasis detection and enhance tumor contrast.

2.1.3 Optical Imaging Technologies

Fluorescence imaging, confocal laser endomicroscopy, and photoacoustic imaging are different optical modalities that allow for real-time noninvasive visualization during both colonoscopy and surgery. These technologies greatly improve tumor margin detection and reduce incomplete resections.

3. Nanotechnology-Based Theranostics

Because nanotechnology can incorporate imaging agents with therapeutic compounds into one nanoscale platform, it is a central component of CRC theranostics.

3.1 Gold Nanoparticles (AuNPs)

AuNPs possess unique optical properties, making them suitable for both CT imaging and photothermal therapy. Their surfaces can also be functionalized with targeting ligands to facilitate tumor selectivity and controlled drug release.

3.2 Liposomes

Liposomal drug carriers, such as liposomal irinotecan, are discussed as biocompatible systems capable of encapsulating chemotherapeutic agents while also serving as imaging

enhancers when modified with contrast molecules. Several liposomal formulations appear in clinical trials.

3.3 Polymeric Nanoparticles

PLGA nanoparticles, PEGylated systems, and dendrimers exhibit high stability, biodegradability, and prolonged circulation. The incorporation of SPIONs or radiotracers within such systems simultaneously offers imaging contrast with the delivery of therapeutic payload.

3.4 Mesoporous Silica Nanoparticles

MSNs possess high loading capacity, tunable pore size, and functionalized surfaces that allow the attachment of ligands. Theranostic MSNs, when labeled with certain isotopes like 177Lu, may enable radiotherapy and SPECT/PET imaging.

3.5 Quantum Dots and Carbon Nanotubes

Quantum dots have excellent fluorescence properties but have toxicity problems. Carbon nanotubes allow for photothermal therapy and drug delivery; their toxicity must be extensively evaluated before clinical use is possible.

4. Targeted Molecular Theranostics in CRC

4.1 EGFR-targeted Systems

Nanoparticles targeting EGFR and radiolabeled monoclonal antibodies increase the precision of therapy, especially for tumors with wild-type KRAS; they also allow for imaging of receptor expression heterogeneity.

4.2 VEGF and Angiogenesis-targeted Approaches

Anti-VEGF agents combined with imaging tracers help to assess the response to antiangiogenic therapy and detect resistant tumor phenotypes.

4.3 c-MET, HGF, and Immune Checkpoint Targets

The review identifies molecular pathways contributing to resistance and outlines emerging theranostic tools such as immuno-PET and checkpoint-directed nanoparticle systems.

5. Toxicity, Regulatory, and Translational Challenges

Despite significant progress in science, several barriers remain:

5.1 Nanotoxicity and Biocompatibility

Long-term toxicity, immunogenicity, genotoxicity, and off-target accumulation remain key concerns. Many nanoparticles show different toxicity profiles in vitro versus in vivo.

5.2 Manufacturing and Scale-Up Limitations

The synthesis of theranostic nanoparticles is often not reproducible, not scalable, and not in accordance with GMP. Further, standardized synthesis and chelator-free radiolabeling are urgently required.

5.3 Regulatory Barriers

Multifunctional platforms challenge the existing regulatory pathways as they function both as imaging agents and drugs. This, in turn, complicates approval processes.

6. Future Directions

The authors underline several priority areas:

1. Standardized toxicity screening protocols

Including cardiac, immunotoxic, and genotoxic assessments for theranostic nanoparticles.

2. Integration of Imaging Biomarkers in Clinical Trials

Therapy dose, schedule, and target selection should be adapted based on real-time imaging.

3. Development of scalable, consistent nanoparticle synthesis

Improved manufacturing approaches, such as pH/redox-responsive and chelator-free radiolabeling systems.

4. Comparative assessments of various imaging modalities

PET/MRI vs PET/CT vs optical systems for tumor detection, surgical navigation, and staging.

7. Clinical Implications

* Improved staging accuracy: PET/MRI and advanced MRI agents improve the detection of lymph-node involvement and micro metastasis.
* Better surgical outcomes: Optical imaging enhances intraoperative tumor visualization and margin clearance.
* Personalized Therapy: Target-specific theranostics are designed for molecular profiles, such as EGFR, VEGF, and immune checkpoint expression.
* Reduced toxicity: Nanocarriers minimize off-target drug effects via controlled release and tumor-targeting accumulation.

* Real-time monitoring: Imaging-guided therapy allows dynamic treatment adjustments based on response.

8. Scope for the Future

- Expanded clinical trials investigating multifunctional nanoparticles in CRC.
- Development of safer, biodegradable, and nonimmunogenic nanomaterials.
- Integration of AI-augmented image analysis with theranostic workflows.
- Exploration of combination modalities, such as magnetic plus optical plus radio-theranostics.
- Personalized therapy algorithms based on imaging signatures and nanoparticle biodistribution.

9. CONCLUSION

Theranostics has emerged as a new paradigm in the management of colorectal cancer, offering great potential for more accurate diagnosis, targeted therapy, and real-time treatment monitoring. Molecular imaging and nanotechnology have resulted in multifunctional platforms that have generated tremendous success in preclinical evaluations. PET/MRI, optical imaging, SPION-based agents, gold nanoparticles, liposomes, polymeric carriers, and mesoporous silica nanoparticles demonstrate the possibility of increasing personalization and improving patient outcomes with theranostics. Clinical translation, however, is presently impeded by hurdles such as toxicity, regulatory complexity, and scalability in manufacturing. These gaps must be addressed in a preclinical manner, using standardized toxicity pipelines, imaging-integrated clinical trial designs, and scalable nanomaterials production processes, in order to translate theranostics from experimental innovations into routine clinical practice.

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