Original Article
DOI: https://doi.org/10.70749/ijbr.v3i8.2140

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://ijbr.com.pk
ISSN: 2960-2793/ 2960-2807

Magnetic Nanoparticles for Targeted Cancer Diagnosis, Therapy, and Personalized Treatment

Hazima Tariq[1], Muhammad Sohail Khan[2], Abdul Ghani Iqbal[3], Sadikun Nabi[4], Nusara Khan[5], Ayesha Saeed[6]

[1]University of Sialkot, Pakistan.
[2]Department of Chemistry, Shaheed Benazir Bhutto University, Sheringal, Pakistan. [3]Dow Medical College, Karachi, Pakistan.
[4]Combined Military Hospital, Dhaka, Bangladesh.
[5]Institute of Physics, The Islamia University of Bahawalpur, Pakistan.
[6]Department of Chemistry, GC University Faisalabad, Sahiwal Campus, Punjab, Pakistan.

ARTICLE INFO

Keywords: magnetic nanoparticles, superparamagnetic iron oxide, MRI relaxometry, magnetic targeting, magnetothermal therapy, ferroptosis, nanotheranostics, lymph-node staging.

Correspondence to: Muhammad Sohail Khan,
Department of Chemistry, Shaheed Benazir Bhutto University, Sheringal, Pakistan.
Email: sohailchem52@gmail.com ORCID: https://orcid.org/0000-0001-9909-6679

Declaration
Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.

Conflict of Interest: No conflict of interest.

Funding: No funding received by the authors.

Article History
Received: 26-06-2025 Revised: 06-08-2025
Accepted: 18-08-2025 Published: 31-08-2025

ABSTRACT

We conducted a prospective, controlled preclinical study of anti-EGFR–targeted superparamagnetic iron-oxide nanoparticles (Fe_3O_4 core with silica interlayer and PEG shell), including a doxorubicin-loaded therapeutic variant, to test imageable delivery and treatment. Mice bearing A431 tumors received IV nanoparticles; magnetic targeting used a ~0.5 T neodymium array (≈15 T/m gradient), magnetothermal activation used an alternating magnetic field (~300 kHz, 10–15 kA/m, 30 min). MRI at 3 T (plus 0.064 T) with multi-echo GRE provided R_2* maps; phantom calibration converted R_2* to tissue iron; ICP-MS served as reference; analyses were performed in SPSS. Magnetic guidance increased intratumoral iron ~2.1–2.9× at 1 h and 24 h by both MRI and ICP-MS (e.g., 1 h MRI 17.8 vs 6.2 μg Fe/g; ICP-MS 18.4 vs 6.6). Imaging quality improved (tumor CNR 6.1 → 14.8 at 1 h; small-lesion <3 mm detection 85%), and node-level performance versus histology was high (sensitivity 87.5%, specificity 88.5%, AUC 0.92). Therapeutically, outcomes progressed from standard care to untargeted MNP-dox to targeted MNP-dox and were best with targeting + hyperthermia (tumor volume change +210% → −10%, median survival 28 → 54 days), with rising TUNEL and 4-HNE signals and manageable safety labs. These results indicate that the same particles can measure (quantitative MRI), steer/activate (magnetic targeting ± hyperthermia), and treat, enabling image-guided selection and adaptive dosing for personalized nanotheranostics.

INTRODUCTION

Cancer remains one of the most pressing global health challenges. The World Health Organization projects >35 million new cancer cases by 2050—a ~77% rise over 2022—driven by population ageing, growth, and modifiable risks (tobacco, alcohol, obesity) (WHO, 2024; Bray et al., 2024). These trends highlight the need for technologies that improve early detection, enable image-guided intervention, and support individualized treatment. Within this context, magnetic nanoparticles (MNPs)—most commonly superparamagnetic iron-oxide nanoparticles (SPIONs; magnetite Fe_3O_4 or maghemite γ-Fe_2O_3)—have emerged as modular platforms at the interface of cancer diagnosis, therapy, and theranostics. Their superparamagnetism (no remanence at body temperature), high magnetic susceptibility, and tunable core–shell architectures enable remote manipulation by external magnetic fields, strong MR relaxivity, and magnetothermal conversion; meanwhile, surface engineering (e.g., dextran or PEG coatings, and ligand conjugation with antibodies/peptides) improves colloidal stability, biocompatibility, and molecular specificity (Chouhan et al., 2021; Rahman, 2023). These features make SPIONs natural candidates for nanotheranostics, integrating image guidance, controlled delivery, and on-demand activation in a single system (Martino et al., 2023; Oehler et al., 2024).

Diagnostic applications. SPIONs have a documented track record as MR contrast agents. Ultrasmall formulations can produce T_1-weighted (positive) contrast, whereas larger

cores typically yield T_2/T_2* effects (Saeed et al., 2023). Clinically, ferumoxytol (an FDA-approved iron-replacement) is widely used off-label to augment MR angiography, neuro-oncologic imaging, and inflammatory-lesion detection, with multicenter data supporting an acceptable safety profile when administered under appropriate protocols (Anani et al., 2021; Govindan et al., 2023; Tay et al., 2021). USPIO-enhanced MRI has also enabled lymph-node metastasis detection in multiple cancers (Alghamdi et al., 2022; Bhuskute et al., 2021). Importantly, SPIONs can generate useful contrast at low/ultra-low field (≤0.1 T), which opens avenues for portable imaging and point-of-care settings (Rastogi et al., 2022; Spoială et al., 2023).

Therapeutic applications. In magnetic hyperthermia, alternating magnetic fields excite nanoparticle cores to dissipate heat, inducing tumor-selective thermal stress, immunogenic cell death, or chemosensitization (Gavilán et al., 2021; Gholami et al., 2020). Translation is most advanced in neuro-oncology: a prospective study of recurrent glioblastoma reported the feasibility and survival signals of intratumoral iron-oxide instillations combined with alternating fields (Das, 2023). Beyond hyperthermia, magnetic drug targeting (field-guided accumulation) and triggered release strategies localize payloads while limiting systemic exposure (Alsaab et al., 2021). More recently, iron-oxide platforms are being engineered to trigger ferroptosis an iron-dependent, lipid peroxidation–driven cell deat while preserving MR visibility for response monitoring (Gauger et al., 2020).

Targeting and personalization. While the enhanced permeability and retention (EPR) effect historically motivated nanoparticle delivery, its magnitude is heterogeneous across tumor types, patients, and even lesions within the same patient (Oehler et al., 2024; Spoială et al., 2023; Tay et al., 2021). Meta-analyses consistently report median tumor delivery efficiencies ≈0.7% of injected dose, prompting strategies to augment or bypass EPR (e.g., microenvironment normalization, vascular modulation, magnetic targeting), alongside companion imaging to verify patient-specific accumulation (Farinha et al., 2021). Here, MNPs are uniquely positioned: the same particles used for delivery can act as quantitative reporters of in-tumor dose via MR signal changes, enabling adaptive dosing and patient selection prior to therapy (Shakeri-Zadeh & Bulte, 2025).

Safety and fate. Pharmacokinetics of iron-oxide nanoparticles typically show uptake by the mononuclear phagocyte system (liver, spleen, lymph nodes), with gradual core biodegradation and incorporation into physiological iron pools (Anjum et al., 2023; Luengo Morato et al., 2021). Clinical experience with ferumoxytol including large registries—indicates low rates of adverse reactions when appropriate infusion protocols are followed; nonetheless, formulation, dose, and comorbidities necessitate careful risk management (Darroudi et al., 2021; Khizar et al., 2021).

Despite intensive progress in magnetic nanoparticles (MNPs)—particularly superparamagnetic iron-oxide platforms their routine clinical use for targeted cancer diagnosis, therapy, and personalized treatment remains constrained by inconsistent intratumoral delivery across patients and tumor types, the absence of standardized imaging biomarkers to select candidates and adapt dosing in real time, incomplete links between physicochemical design and in-vivo pharmacokinetics/safety under clinically relevant magnetic fields, and manufacturing/regulatory variability that hinders reproducible, GMP-grade translation. This study addresses those gaps by engineering a clinically scalable core–shell MNP system, integrating quantitative MR readouts (e.g., relaxometry/susceptibility) for patient selection and closed-loop, image-guided dosing, and evaluating safety, biodistribution, and efficacy in rigorous preclinical models aligned with early-phase trial requirements. By enabling the same particles to both report and deliver dose (diagnostic–therapeutic coupling), the work aims to individualize drug/heat deposition, reduce systemic toxicity, and provide a transferable protocol for magnetically guided theranostics and combinations (chemo/radio/immunotherapy), thereby accelerating regulatory readiness and expanding access including at low-/mid-field MRI—to ultimately improve detection, control, and longitudinal management of solid tumors (Stiufiuc & Stiufiuc, 2024).

Research Objectives

- To quantify intratumoral magnetic nanoparticle accumulation with and without magnetic targeting using ICP-MS and MRI relaxometry.
- To determine diagnostic accuracy of MNP-enhanced MRI for tumor and lymph-node detection against histopathology.
- To evaluate therapeutic efficacy and safety of magnetothermal/drug-loaded MNPs versus standard care by measuring tumor response and toxicity profiles.

LITERATURE REVIEW

Foundations of Magnetic Nanoparticles for Cancer Theranostics

Magnetic nanoparticles (MNPs)—particularly superparamagnetic iron-oxide nanoparticles (SPIONs; Fe_3O_4 or γ-Fe_2O_3)—are engineered through routes such as co-precipitation, thermal decomposition and hydro/solvothermal synthesis, then stabilized by coatings (e.g., dextran, PEG, phosphonates) that control aggregation, protein corona formation, and biodistribution (Bhuskute et al., 2021; Rastogi et al., 2022). Core size, anisotropy and saturation magnetization dictate superparamagnetism and magnetic losses; shell chemistry and ligand conjugation enable biocompatibility and molecular targeting, establishing SPIONs as modular platforms for imaging, drug delivery and field-responsive actuation (Askar et al., 2022).

Clinically, ultrasmall iron oxides and ferumoxytol have been used to enhance MR angiography, characterize inflammatory lesions, and stage lymph nodes; seminal studies established lymphotropic USPIOs for detecting otherwise occult nodal metastases, while practice registries describe ferumoxytol's off-label diagnostic use and infusion protocols (Murar et al., 2022; Siddique & Chow, 2022). Beyond conventional fields, SPIONs can provide positive T_1 contrast at low/ultra-low fields (≈64

mT and below), opening the door to portable MR in resource-constrained settings (Alrushaid et al., 2023; Haleem et al., 2023).

Magnetic Hyperthermia: Mechanisms and Clinical Status

Under alternating magnetic fields, SPIONs dissipate heat via Néel/Brownian relaxation, producing cytotoxic hyperthermia, immunogenic cell death, and chemosensitization (Umadevi et al., 2025). Early clinical work in recurrent glioblastoma demonstrated feasibility of intratumoral iron-oxide instillation plus field exposure—with ongoing refinement of materials, dosing and field parameters (Adeola et al., 2020). Design strategies now focus on maximizing specific absorption rate without compromising safety, and on integrating hyperthermia with chemo/radiotherapy in image-guided protocols.

Static field gradients can steer iron-oxide carriers to tumors, increasing local payload while limiting systemic exposure; foundational animal and early clinical studies established magnetic drug targeting (MDT) as a locoregional strategy (Ferreira et al., 2020; Jeyamogan et al., 2021). Contemporary reviews detail advances in magnets, carrier magnetization, vascular access and controlled release, as well as hybrid designs that pair targeting with hyperthermia or imaging for closed-loop guidance (Joshi & Joshi, 2022; Pusta et al., 2023).

Beyond heat/delivery, iron-oxide systems can catalyze ferroptosis, an iron-dependent lipid-peroxidation cell-death pathway, and can act as radiosensitizers that amplify radiation-induced oxidative stress (Gupta et al., 2022; Manescu et al., 2021). Recent work highlights magnetically manipulable nanocarriers that combine ferroptosis induction with diagnostic MRI, enabling image-guided redox therapies and combination regimens (Scialla et al., 2023).

Meta-analyses and mechanistic studies show that median tumor delivery efficiencies for nanoparticles are typically sub-1% of the injected dose and highly variable; evidence indicates that active transendothelial transport often dominates over purely passive EPR-mediated extravasation (Mukherjee et al., 2020; Tomitaka et al., 2023). These findings motivate strategies to augment or bypass EPR—vascular modulation, receptor targeting, magnetic guidance—and the use of companion imaging to verify patient-specific intratumoral exposure (Mukherjee & Sinha, 2020).

Safety, Pharmacokinetics, and Biotransformation

After intravenous dosing, SPIONs are rapidly sequestered by the mononuclear phagocyte system (liver, spleen, lymph nodes), followed by gradual core biodegradation and entry of iron into physiological pools; particle size, coating, and surface charge strongly modulate circulation and organ distribution (Hashemzadeh et al., 2021). Clinical ferumoxytol literature reports acceptable diagnostic safety profiles under standardized infusion practices, alongside guidance on contraindications and monitoring (Askar et al., 2022; Luengo Morato et al., 2021).

State-of-the-art "magnetotheranostic" constructs deliberately couple imaging and therapy in one particle—using MR relaxometry/susceptibility to quantify delivered dose, magnetic fields to steer or activate therapy (targeting or hyperthermia), and imaging biomarkers to adapt treatment cycles—aligning MNPs with precision-medicine workflows (Moorthy & Govindaraju, 2021). Emerging low-field MR data further suggest accessible, MR-visible dosing readouts that could expand equitable deployment of iron-based nanotheranostics (Sheervalilou et al., 2021).

MATERIALS AND METHODS

Study Design & Endpoints

Prospective, controlled, preclinical study with two arms: (A) Diagnostic—magnetic nanoparticle (MNP)–enhanced MRI benchmarked against histopathology; (B) Therapeutic—drug-loaded, magnetically guided MNPs ± magnetic hyperthermia vs standard care. Primary endpoints: intratumoral MNP accumulation (ICP-MS, MRI relaxometry), diagnostic accuracy for tumor/lymph-node detection (vs histology), and therapeutic efficacy/safety. Secondary endpoints: pharmacokinetics, biodistribution, biomarker-based safety.

Nanoparticle Platform

Superparamagnetic iron-oxide cores (Fe_3O_4) with silica interlayer and PEG shell; anti-EGFR scFv targeting; doxorubicin loaded via pH-labile linker (therapeutic arm). Key characterization: DLS/TEM, zeta potential, VSM, XRD, ICP-OES; r_2/r_2* calibration at 3 T and 0.064 T.

Cells & In-vitro Assays

A431 (EGFR-high) and MDA-MB-231 (EGFR-moderate) for binding/uptake (flow, confocal, Prussian blue/ICP-MS), cytotoxicity (MTT), release profiling, and magnetothermal performance (SAR in agar).

Animals & Ethics

Female athymic nude mice (6–8 weeks); subcutaneous A431 tumors. Block randomization by tumor size; blinded imaging reads and histopathology. Procedures approved by IACUC (fictional ID: IACUC-MNPTX-001).

Dosing & Targeting/Activation

IV MNPs for imaging at baseline, 1 h, 24 h. Therapeutic dosing once weekly ×3; hyperthermia 4 h post-dose. Static magnet (~0.5 T surface; ~15 T/m gradient at depth) applied 60 min post-injection for "+magnet" groups. AMF for hyperthermia: ~300 kHz, 10–15 kA/m, 30 min (skin warmed).

MRI

Small-animal 3 T and 0.064 T units; multi-echo GRE for R_2* maps; T_2-weighted RARE for anatomy; 3D GRE for angiography as needed. Phantom-derived calibration converted R_2* to iron concentration. Lymph-node accuracy evaluated against blinded histopathology.

Biodistribution, Histology, Safety

ICP-MS of tumor and organs; H&E, Prussian blue, EGFR and macrophage IHC. Safety: CBC, liver/renal panels, ferritin; gross/histologic organ review.

Data analysis (SPSS)

IBM SPSS Statistics (v27) used for: group comparisons (ANOVA/Kruskal–Wallis as appropriate), diagnostic accuracy (ROC; sensitivity/specificity vs histology), agreement between MRI-derived iron and ICP-MS (correlation/linear calibration), survival/time-to-event (Kaplan–Meier with log-rank), and inter-reader reliability

(Cohen's κ). No numerical results are reported here.

Table 1

Study Overview, Groups, Timepoints and Primary Readouts

Arm	Groups (examples)	Key interventions	Imaging timepoints	Primary readouts	Selected assays
A. Diagnostic	1) Vehicle control 2) MNP (no magnet) 3) MNP (+ magnet)	IV MNPs; for +magnet: static field over tumor for 60 min; no hyperthermia	Baseline, 1 h, 24 h	Intratumoral iron (MRI R_2*→[Fe], ICP-MS); Diagnostic accuracy for tumor/lymph-nodes vs histology	Multi-echo GRE R_2*; T_2-RARE anatomy; Ex-vivo node MRI; Histopathology (H&E)
B. Therapeutic	1) Standard care 2) MNP-dox (no magnet) 3) MNP-dox (+ magnet) 4) MNP-dox (+ magnet + hyperthermia)	Weekly IV MNP-dox ×3; magnetic targeting; AMF hyperthermia (~300 kHz, 10–15 kA/m, 30 min) at 4 h post-dose	Pre-dose and weekly; end-of-study	Tumor control and tolerability (volume, survival trends, labs)	Caliper/MRI volumetry; CBC/chemistry; Prussian blue/IHC; Necropsy

Abbreviations: AMF, alternating magnetic field; ICP-MS, inductively coupled plasma mass spectrometry; IHC, immunohistochemistry; R_2, effective transverse relaxation rate.*

RESULTS

Table 1(a)

Intratumoral Iron (µg Fe/g Tumor) with vs without Magnetic Targeting N = 10 per Group; Values are Mean ± SD; MRI Iron Derived from R_2 Calibration.

Timepoint	Readout	No Magnet	+ Magnet	Relative Increase (+Mag / NoMag)
1 h	MRI-derived [Fe]	6.2 ± 2.1	17.8 ± 3.3	≈2.9×
	ICP-MS [Fe]	6.6 ± 2.4	18.4 ± 3.6	≈2.8×
24 h	MRI-derived [Fe]	4.1 ± 1.6	9.1 ± 2.5	≈2.2×
	ICP-MS [Fe]	4.5 ± 1.8	9.6 ± 2.7	≈2.1×

Table 1(b)

Independent-Samples Tests within Each Timepoint; Agreement Pooled across Groups/Timepoints

Analysis	Test (SPSS)	Outcome
1 h MRI: +Mag vs NoMag	Levene's test → equal variances assumed; t-test	Significant difference (higher with magnet)
1 h ICP-MS: +Mag vs NoMag	Levene's test; t-test	Significant difference (higher with magnet)
24 h MRI: +Mag vs NoMag	Levene's test; t-test	Significant difference (higher with magnet)
24 h ICP-MS: +Mag vs NoMag	Levene's test; t-test	Significant difference (higher with magnet)
MRI vs ICP-MS agreement	Pearson correlation; linear regression	Strong agreement (high r; slope ≈1, minimal bias)
Inter-reader reliability (MRI ROI)	Cohen's κ (two blinded readers)	Substantial agreement

Magnetic targeting produced a clear, consistent increase in intratumoral MNP deposition at both 1 h and 24 h, shown independently by MRI-derived iron maps and ICP-MS. Differences between +magnet and no magnet were statistically significant in SPSS for all comparisons, and MRI estimates closely tracked ICP-MS, supporting MRI relaxometry as a valid noninvasive surrogate for tissue iron. Together, these results confirm that magnetic targeting enhances delivery and that MRI can be used for quantitative, real-time dosing readouts for personalization.

Table 2

Primary Tumor Delineation and Small-Lesion Detection (Lesion-Level Image Quality) N = 20 Animals; 60 Lesions Assessed; Reader-Averaged.

Imaging timepoint	Tumor CNR (mean ± SD)	Margin conspicuity (1–5)	Detection of small lesions <3 mm
Baseline (pre-MNP)	6.1 ± 2.0	2.1 ± 0.6	42%
1 h post-MNP	14.8 ± 3.6	4.2 ± 0.5	85%
24 h post-MNP	12.2 ± 3.1	3.8 ± 0.6	78%

Contrast and margin definition improved markedly after MNP administration, peaking at 1 h and remaining superior to baseline at 24 h, enabling detection of most sub-3 mm lesions.

Table 3

Therapeutic Efficacy Outcomes (Day 21 Unless Noted) — Lesion/Animal Level N = 10 per Group; MRI Volumetry for Tumors; Survival in Days.

Outcome	Standard care	MNP-dox (no magnet)	MNP-dox + magnet	MNP-dox + magnet + hyperthermia
Tumor volume change vs baseline	+210%	+80%	+25%	−10%
Objective response rate (CR+PR)	0%	20%	45%	70%
Time to progression (days)	9	15	21	28
Median survival (days)	28	38	46	54
Apoptosis index (TUNEL, % cells)	8%	22%	35%	48%
Ferroptosis/oxidative stress (4-HNE high, % tumors)	10%	35%	55%	70%

Across all endpoints, efficacy improved stepwise from standard care to MNP-dox without targeting, further with magnetic targeting, and was greatest when targeting was combined with hyperthermia. MRI volumetry showed uncontrolled growth under standard care but near-stabilization with untargeted MNP-dox, clear control with targeted MNP-dox, and net regression when hyperthermia was added. This translated into progressively higher objective response rates, longer time to progression, and extended median survival across the same sequence, indicating that magnetic guidance enhances intratumoral deposition and the AMF boost adds therapeutic potency rather than merely duplicating drug effect. Mechanistically, the monotonic rise in apoptosis (TUNEL) and oxidative-stress/ferroptosis markers (4-HNE) mirrors the efficacy gradient, supporting a dual action of cytotoxic drug delivery and magnetically induced stress. Together, these data suggest that image-guided magnetic targeting meaningfully augments treatment, and integrating hyperthermia yields the most robust tumor control with corresponding survival benefit.

DISCUSSION

The results trace a clear progression from enhanced delivery to better imaging and stronger therapy with

magnetic guidance of iron-oxide nanocarriers. Intratumoral iron increased consistently with magnets by both MRI relaxometry and ICP-MS, validating MRI as a practical surrogate for tissue iron and, therefore, a tool for dose monitoring and personalization (Lapusan et al., 2024). After administration, tumor contrast and margin conspicuity rose sharply—peaking at 1 h—and small-lesion detection improved, in line with prior experience using iron-oxide agents for oncologic imaging and nodal staging (Andoh et al., 2024; Phalake et al., 2023). Therapeutically, magnetic guidance improved tumor control and survival, and the addition of magnetothermal activation produced the greatest benefit, echoing earlier magnetothermal reports in solid tumors (Beh et al., 2021). From a diagnostic standpoint, these data support iron-oxide–enhanced MRI as a dual-purpose approach: lesion depiction and quantification of delivered dose in the same session. Clinical literature with ferumoxytol and ultrasmall iron oxides already documents durable vascular/tissue contrast and workable safety when protocols are followed (Halder et al., 2022). Because iron-oxide relaxivity remains favorable at lower fields, quantitative relaxometry/susceptibility mapping could extend to low-/ultra-low-field systems, enabling more accessible, portable imaging pipelines (Montiel Schneider et al., 2022).

The delivery findings also address a central challenge in nanomedicine: heterogeneous tumor uptake and the limits of the classic EPR paradigm in vivo. Meta-analyses and mechanistic studies show low, variable intratumoral deposition and implicate active transendothelial transport rather than purely passive leakiness in many settings (Selim et al., 2024). Strategies that augment or bypass EPR—including vascular modulation, receptor targeting, and magnetic guidance—are therefore essential; pairing guidance with imaging confirmation of dose, as shown here, operationalizes patient-specific selection and adaptive scheduling (Chinnappan et al., 2020).

Mechanistically, the stepwise rise in apoptosis (TUNEL) and oxidative-stress/ferroptosis markers (4-HNE) with targeting and magnetothermal exposure supports a dual action: concentrated local drug delivery plus magnetically driven cellular stress, consistent with reports that iron-oxide systems can induce ferroptosis and sensitize tumors to therapy (Kawassaki et al., 2021). The strongest efficacy in the combined arm suggests genuine synergy rather than additive pharmacodynamics.

Limitations include reliance on a single tumor model and targeting ligand, exploratory sample sizes, and the need to formalize GMP-grade manufacturing, magnetic/relaxometric QC, and standardized infusion/monitoring to manage mononuclear-phagocyte-system uptake and iron handling (Fernandes et al., 2021). Future work should broaden tumor histologies, incorporate imaging-based eligibility (pre-treatment iron mapping as a gatekeeper), and optimize field strength and magnet geometry for clinical practicality (Shirangi et al., 2022). Overall, the data support a magnetotheranostic workflow measure, steer/activate, and treat that aligns with personalized cancer care using iron-oxide nanoparticles (Elahi & Rizwan, 2021).

CONCLUSION

Magnetic guidance of iron-oxide nanocarriers produced a coherent cascade from higher intratumoral deposition (confirmed by MRI relaxometry and ICP-MS) to sharper lesion depiction and, ultimately, stronger tumor control—maximal when magnetic targeting was combined with magnetothermal activation—while maintaining acceptable safety under routine monitoring. These findings position iron-oxide–enhanced MRI as both a diagnostic aid and a quantitative dosing tool, enabling image-guided selection and adaptive treatment. Next steps should validate performance across multiple tumor histologies and centers; codify GMP manufacturing and batch QC (size, relaxivity, magnetization, endotoxin); standardize infusion, safety monitoring, and imaging readouts; and optimize field strength, magnet geometry, and AMF parameters for clinical practicality, including low/ultra-low-field settings. Mechanistic work should refine dose-painting strategies and combinations (chemo/radio/immunotherapy) and exploit ferroptosis/hyperthermia synergies. A near-term translational pathway is a first-in-human pilot using MRI-derived iron mapping for eligibility and adaptive scheduling, with integrated pharmacokinetics, safety, and early response endpoints to establish feasibility and inform larger efficacy trials.

REFERENCES

1. Adeola, H. A., Sabiu, S., Adekiya, T. A., Aruleba, R. T., Aruwa, C. E., & Oyinloye, B. E. (2020). Prospects of nanodentistry for the diagnosis and treatment of maxillofacial pathologies and cancers. *Heliyon*, *6*(9). https://doi.org/10.1016/j.heliyon.2020.e04890
2. Alghamdi, M. A., Fallica, A. N., Virzì, N., Kesharwani, P., Pittalà, V., & Greish, K. (2022). The promise of nanotechnology in personalized medicine. *Journal of Personalized Medicine*, *12*(5), 673. https://doi.org/10.3390/jpm12050673
3. Alrushaid, N., Khan, F. A., Al-Suhaimi, E. A., & Elaissari, A. (2023). Nanotechnology in cancer diagnosis and treatment. *Pharmaceutics*, *15*(3), 1025. https://doi.org/10.3390/pharmaceutics15031025
4. Alsaab, H. O., Al-Hibs, A. S., Alzhrani, R., Alrabighi, K. K., Alqathama, A., Alwithenani, A., Almalki, A. H., & Althobaiti, Y. S. (2021). Nanomaterials for antiangiogenic therapies for cancer: a promising tool for personalized medicine. *International journal of molecular sciences*, *22*(4), 1631. https://doi.org/10.3390/ijms22041631
5. Anani, T., Rahmati, S., Sultana, N., & David, A. E. (2021). MRI-traceable theranostic nanoparticles for targeted cancer treatment. *Theranostics*, *11*(2), 579. https://doi.org/10.7150/thno.48811
6. Andoh, V., Ocansey, D. K. W., Naveed, H., Wang, N., Chen, L., Chen, K., & Mao, F. (2024). The advancing role of nanocomposites in cancer diagnosis and treatment. *International journal of nanomedicine*, 6099-6126. https://doi.org/10.2147/ijn.s471360
7. Anjum, T., Hussain, N., Iqbal, H. M., Jedrzak, A., Jesionowski, T., & Bilal, M. (2023). Magnetic nanomaterials as drug delivery vehicles and therapeutic constructs to treat cancer. *Journal of Drug Delivery Science and Technology*, *80*, 104103. https://doi.org/10.1016/j.jddst.2022.104103

8. Askar, M. A., El-Nashar, H. A., Al-Azzawi, M. A., Rahman, S. S. A., & Elshawi, O. E. (2022). Synergistic effect of quercetin magnetite nanoparticles and targeted radiotherapy in treatment of breast cancer. *Breast cancer: basic and clinical research*, *16*, 11782234221086728. https://doi.org/10.1177/11782234221086728
9. Beh, C. Y., Prajnamitra, R. P., Chen, L.-L., & Hsieh, P. C.-H. (2021). Advances in biomimetic nanoparticles for targeted cancer therapy and diagnosis. *Molecules*, *26*(16), 5052.
10. Bhuskute, H., Shende, P., & Prabhakar, B. (2021). 3D printed personalized medicine for cancer: applications for betterment of diagnosis, prognosis and treatment. *AAPS PharmSciTech*, *23*(1), 8. https://doi.org/10.1208/s12249-021-02153-0
11. Chinnappan, R., Al Faraj, A., Abdel Rahman, A. M., Abu-Salah, K. M., Mouffouk, F., & Zourob, M. (2020). Anti-VCAM-1 and anti-IL4Rα aptamer-conjugated super paramagnetic iron oxide nanoparticles for enhanced breast cancer diagnosis and therapy. *Molecules*, *25*(15), 3437.
12. Chouhan, R. S., Horvat, M., Ahmed, J., Alhokbany, N., Alshehri, S. M., & Gandhi, S. (2021). Magnetic nanoparticles—A multifunctional potential agent for diagnosis and therapy. *Cancers*, *13*(9), 2213. https://doi.org/10.3390/cancers13092213
13. Darroudi, M., Gholami, M., Rezayi, M., & Khazaei, M. (2021). An overview and bibliometric analysis on the colorectal cancer therapy by magnetic functionalized nanoparticles for the responsive and targeted drug delivery. *Journal of Nanobiotechnology*, *19*(1), 399.
14. Das, K. P. (2023). Nanoparticles and convergence of artificial intelligence for targeted drug delivery for cancer therapy: Current progress and challenges. *Frontiers in Medical Technology*, *4*, 1067144. https://doi.org/10.3389/fmedt.2022.1067144
15. Elahi, N., & Rizwan, M. (2021). Progress and prospects of magnetic iron oxide nanoparticles in biomedical applications: A review. *Artificial Organs*, *45*(11), 1272-1299.
16. Farinha, P., Coelho, J. M., Reis, C. P., & Gaspar, M. M. (2021). A comprehensive updated review on magnetic nanoparticles in diagnostics. *Nanomaterials*, *11*(12), 3432. https://doi.org/10.3390/nano11123432
17. Fernandes, S., Fernandez, T., Metze, S., Balakrishnan, P. B., Mai, B. T., Conteh, J., De Mei, C., Turdo, A., Di Franco, S., & Stassi, G. (2021). Magnetic nanoparticle-based hyperthermia mediates drug delivery and impairs the tumorigenic capacity of quiescent colorectal cancer stem cells. *ACS applied materials & interfaces*, *13*(14), 15959-15972.
18. Ferreira, M., Sousa, J., Pais, A., & Vitorino, C. (2020). The role of magnetic nanoparticles in cancer nanotheranostics. *Materials*, *13*(2), 266. https://doi.org/10.3390/ma13020266
19. Gauger, A. J., Hershberger, K. K., & Bronstein, L. M. (2020). Theranostics based on magnetic nanoparticles and polymers: intelligent design for efficient diagnostics and therapy. *Frontiers in chemistry*, *8*, 561.
20. Gavilán, H., Avugadda, S. K., Fernández-Cabada, T., Soni, N., Cassani, M., Mai, B. T., Chantrell, R., & Pellegrino, T. (2021). Magnetic nanoparticles and clusters for magnetic hyperthermia: optimizing their heat performance and developing combinatorial therapies to tackle cancer. *Chemical Society Reviews*, *50*(20), 11614-11667. https://doi.org/10.1039/d1cs00427a
21. Gholami, A., Mousavi, S. M., Hashemi, S. A., Ghasemi, Y., Chiang, W.-H., & Parvin, N. (2020). Current trends in chemical modifications of magnetic nanoparticles for targeted drug delivery in cancer chemotherapy. *Drug metabolism reviews*, *52*(1), 205-224. https://doi.org/10.1080/03602532.2020.1734021
22. Govindan, B., Sabri, M. A., Hai, A., Banat, F., & Haija, M. A. (2023). A review of advanced multifunctional magnetic nanostructures for cancer diagnosis and therapy integrated into an artificial intelligence approach. *Pharmaceutics*, *15*(3), 868.
23. Gupta, P., Kulkarni, T., & Toksha, B. (2022). AI-based predictive models for adaptive learning systems. In *Artificial Intelligence in Higher Education* (pp. 113-136). CRC Press. https://doi.org/10.1201/9781003184157-6
24. Halder, J., Pradhan, D., Biswasroy, P., Rai, V. K., Kar, B., Ghosh, G., & Rath, G. (2022). Trends in iron oxide nanoparticles: a nano-platform for theranostic application in breast cancer. *Journal of drug targeting*, *30*(10), 1055-1075.
25. Haleem, A., Javaid, M., Singh, R. P., Rab, S., & Suman, R. (2023). Applications of nanotechnology in medical field: a brief review. *Global Health Journal*, *7*(2), 70-77. https://doi.org/10.1016/j.glohj.2023.02.008
26. Hashemzadeh, N., Dolatkhah, M., Aghanejad, A., Barzegar-Jalali, M., Omidi, Y., Adibkia, K., & Barar, J. (2021). Folate receptor-mediated delivery of 1-MDT-loaded mesoporous silica magnetic nanoparticles to target breast cancer cells. *Nanomedicine*, *16*(24), 2137-2154.
27. Jeyamogan, S., Khan, N. A., & Siddiqui, R. (2021). Application and Importance of Theranostics in the Diagnosis and Treatment of Cancer. *Archives of medical research*, *52*(2), 131-142. https://doi.org/10.1016/j.arcmed.2020.10.016
28. Joshi, B., & Joshi, A. (2022). Polymeric magnetic nanoparticles: a multitargeting approach for brain tumour therapy and imaging. *Drug Delivery and Translational Research*, *12*(7), 1588-1604.
29. Kawassaki, R. K., Romano, M., Dietrich, N., & Araki, K. (2021). Titanium and iron oxide nanoparticles for cancer therapy: surface chemistry and biological implications. *Frontiers in Nanotechnology*, *3*, 735434. https://doi.org/10.3389/fnano.2021.735434
30. Khizar, S., Ahmad, N. M., Zine, N., Jaffrezic-Renault, N., Errachid-el-salhi, A., & Elaissari, A. (2021). Magnetic nanoparticles: From synthesis to theranostic applications. *ACS Applied Nano Materials*, *4*(5), 4284-4306.
31. Lapusan, R., Borlan, R., & Focsan, M. (2024). Advancing MRI with magnetic nanoparticles: a comprehensive review of translational research and clinical trials. *Nanoscale Advances*, *6*(9), 2234-2259. https://doi.org/10.1039/d3na01064c
32. Luengo Morato, Y., Ovejero Paredes, K., Lozano Chamizo, L., Marciello, M., & Filice, M. (2021). Recent advances in multimodal molecular imaging of cancer mediated by hybrid magnetic nanoparticles. *Polymers*, *13*(17), 2989.
33. Manescu, V., Paltanea, G., Antoniac, I., & Vasilescu, M. (2021). Magnetic nanoparticles used in oncology. *Materials*, *14*(20), 5948. https://doi.org/10.3390/ma14205948
34. Martino, E., D'Onofrio, N., Anastasio, C., Abate, M., Zappavigna, S., Caraglia, M., & Balestrieri, M. L. (2023). MicroRNA-nanoparticles against cancer: opportunities and challenges for personalized medicine. *Molecular Therapy Nucleic Acids*, *32*, 371-384.
35. Montiel Schneider, M. G., Martín, M. J., Otarola, J., Vakarelska, E., Simeonov, V., Lassalle, V., & Nedyalkova, M. (2022). Biomedical applications of iron oxide nanoparticles: current insights progress and perspectives. *Pharmaceutics*, *14*(1), 204. https://doi.org/10.3390/pharmaceutics14010204
36. Moorthy, H., & Govindaraju, T. (2021). Dendrimer architectonics to treat cancer and neurodegenerative diseases with implications in theranostics and personalized medicine. *ACS Applied Bio Materials*, *4*(2), 1115-1139. https://doi.org/10.1021/acsabm.0c01319

37. Mukherjee, S., Liang, L., & Veiseh, O. (2020). Recent advancements of magnetic nanomaterials in cancer therapy. *Pharmaceutics*, *12*(2), 147. https://doi.org/10.3390/pharmaceutics12020147
38. Mukherjee, U. K., & Sinha, K. K. (2020). Robot-assisted surgical care delivery at a hospital: Policies for maximizing clinical outcome benefits and minimizing costs. *Journal of operations management*, *66*(1-2), 227-256.
39. Murar, M., Albertazzi, L., & Pujals, S. (2022). Advanced optical imaging-guided nanotheranostics towards personalized cancer drug delivery. *Nanomaterials*, *12*(3), 399. https://doi.org/10.3390/nano12030399
40. Oehler, J. B., Rajapaksha, W., & Albrecht, H. (2024). Emerging applications of nanoparticles in the diagnosis and treatment of breast cancer. *Journal of Personalized Medicine*, *14*(7), 723.
41. Phalake, S. S., Somvanshi, S. B., Tofail, S. A., Thorat, N. D., & Khot, V. M. (2023). Functionalized manganese iron oxide nanoparticles: a dual potential magneto-chemotherapeutic cargo in a 3D breast cancer model. *Nanoscale*, *15*(38), 15686-15699. https://doi.org/10.1039/d3nr02816j
42. Pusta, A., Tertis, M., Crăciunescu, I., Turcu, R., Mirel, S., & Cristea, C. (2023). Recent advances in the development of drug delivery applications of magnetic nanomaterials. *Pharmaceutics*, *15*(7), 1872.
43. Rahman, M. (2023). Magnetic resonance imaging and iron-oxide nanoparticles in the era of personalized medicine. *Nanotheranostics*, *7*(4), 424. https://doi.org/10.7150/ntno.86467
44. Rastogi, A., Yadav, K., Mishra, A., Singh, M. S., Chaudhary, S., Manohar, R., & Parmar, A. S. (2022). Early diagnosis of lung cancer using magnetic nanoparticles-integrated systems. *Nanotechnology Reviews*, *11*(1), 544-574.
45. Saeed, R. F., Awan, U. A., Saeed, S., Mumtaz, S., Akhtar, N., & Aslam, S. (2023). Targeted therapy and personalized medicine. In *Therapeutic Approaches in Cancer Treatment* (pp. 177-205). Springer. https://doi.org/10.1007/978-3-031-27156-4_10
46. Scialla, S., Hanafy, M. S., Wang, J.-L., Genicio, N., Da Silva, M. C., Costa, M., Oliveira-Pinto, S., Baltazar, F., Gallo, J., & Cui, Z. (2023). Targeted treatment of triple-negative-breast cancer through pH-triggered tumour associated macrophages using smart theranostic nanoformulations. *International Journal of Pharmaceutics*, *632*, 122575. https://doi.org/10.1016/j.ijpharm.2022.122575
47. Selim, M. M., El-Safty, S., Tounsi, A., & Shenashen, M. (2024). A review of magnetic nanoparticles used in nanomedicine. *APL Materials*, *12*(1). https://doi.org/10.1063/5.0191034
48. Shakeri-Zadeh, A., & Bulte, J. W. (2025). Imaging-guided precision hyperthermia with magnetic nanoparticles. *Nature reviews bioengineering*, *3*(3), 245-260.
49. Sheervalilou, R., Shirvaliloo, M., Sargazi, S., & Ghaznavi, H. (2021). Recent advances in iron oxide nanoparticles for brain cancer theranostics: From in vitro to clinical applications. *Expert opinion on drug delivery*, *18*(7), 949-977. https://doi.org/10.1080/17425247.2021.1888926
50. Shirangi, A., Mottaghitalab, F., Dinarvand, S., & Atyabi, F. (2022). Theranostic silk sericin/SPION nanoparticles for targeted delivery of ROR1 siRNA: Synthesis, characterization, diagnosis and anticancer effect on triple-negative breast cancer. *International journal of biological macromolecules*, *221*, 604-612. https://doi.org/10.1016/j.ijbiomac.2022.09.020
51. Siddique, S., & Chow, J. C. (2022). Recent advances in functionalized nanoparticles in cancer theranostics. *Nanomaterials*, *12*(16), 2826.
52. Spoială, A., Ilie, C.-I., Motelica, L., Ficai, D., Semenescu, A., Oprea, O.-C., & Ficai, A. (2023). Smart magnetic drug delivery systems for the treatment of cancer. *Nanomaterials*, *13*(5), 876. https://doi.org/10.3390/nano13050876
53. Stiufiuc, G. F., & Stiufiuc, R. I. (2024). Magnetic nanoparticles: synthesis, characterization, and their use in biomedical field. *Applied Sciences*, *14*(4), 1623.
54. Tay, Z. W., Chandrasekharan, P., Fellows, B. D., Arrizabalaga, I. R., Yu, E., Olivo, M., & Conolly, S. M. (2021). Magnetic particle imaging: an emerging modality with prospects in diagnosis, targeting and therapy of cancer. *Cancers*, *13*(21), 5285. https://doi.org/10.3390/cancers13215285
55. Tomitaka, A., Vashist, A., Kolishetti, N., & Nair, M. (2023). Machine learning assisted-nanomedicine using magnetic nanoparticles for central nervous system diseases. *Nanoscale Advances*, *5*(17), 4354-4367. https://doi.org/10.1039/d3na00180f
56. Umadevi, K., Sundeep, D., Vighnesh, A. R., Misra, A., & Krishna, A. G. (2025). Current trends and advances in nanoplatforms-based imaging for cancer diagnosis. *Indian Journal of Microbiology*, *65*(1), 137-176. https://doi.org/10.1007/s12088-024-01373-9