The Review Of
DIABETIC
STUDIES OPEN ACCESS

The Biomarker-Imaging Feedback Loop: A Narrative Review of Integrated Diagnostics in Oncology and Autoimmune Disease

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Abstract

Background: The management of complex chronic diseases like metastatic cancer and systemic autoimmune conditions relies on the dynamic interplay between laboratory-derived biomarkers and radiological imaging. This interdependent relationship forms a critical diagnostic and therapeutic feedback loop that guides clinical decision-making.
Aim: This narrative review aims to synthesize evidence on the integrated use of serological biomarkers and medical imaging in the Internal Medicine-led management of oncology and autoimmune diseases, focusing on the systemic coordination required for effective monitoring.
Methods: A comprehensive literature search was conducted in PubMed, Scopus, Web of Science, and CINAHL (2010-2024), incorporating clinical, technological, and health services research perspectives.
Results: The review identifies that optimal disease management depends on the temporal synchronization and interpretive synthesis of biomarker and imaging data. Successful integration is hampered by information silos, asynchronous testing schedules, and fragmented coordination. The implementation of unified data dashboards and the strategic deployment of health assistants for logistical coordination significantly enhance the functionality of this diagnostic loop.
Conclusion: The biomarker-imaging feedback loop is a cornerstone of modern chronic disease management. Its effectiveness requires deliberate system-level integration, including technological interoperability and redesigned care coordination roles.

Keywords: precision medicine; tumor markers; medical imaging; care coordination; chronic disease management.

Introduction

The paradigm of chronic disease management, particularly in oncology and autoimmune disorders, has evolved from static diagnosis and linear treatment pathways to a dynamic, surveillance-intensive model (Larkin et al., 2022). This evolution is driven by the recognition that diseases such as metastatic cancer and rheumatoid arthritis are not static entities but biologically active processes that fluctuate over time

in response to treatment, disease evolution, and host factors (Das et al., 2023). Effective management in this context requires continuous monitoring through two complementary diagnostic lenses: the molecular and the anatomical. Serological biomarkers—proteins, autoantibodies, genetic fragments, and inflammatory indices detectable in blood and other bodily fluids—provide a molecular narrative of disease activity, offering insights into cellular processes, treatment response, and early signs of resistance or flare (Holdenrieder et al., 2016). Concurrently, advanced medical imaging technologies—including computed tomography (CT), positron emission tomography (PET), and magnetic resonance imaging (MRI)—deliver an anatomical and functional narrative, visualizing tumor burden, metastatic spread, synovial inflammation, and structural damage with increasing precision (Aide et al., 2017).

The interdependence of these data streams creates what this review terms the biomarker-imaging feedback loop. This is not a simple sequence of tests but an iterative cycle where imaging findings prompt biomarker investigation (e.g., a new liver lesion prompting a carcinoembryonic antigen [CEA] test), and rising biomarkers trigger targeted imaging (e.g., rising anti-cyclic citrullinated peptide [anti-CCP] antibodies prompting a joint ultrasound) (Shekari et al., 2023). The clinical decision—to continue, modify, or cease therapy—hinges on the synthesized interpretation of this combined data by the treating internist or specialist (Wang et al., 2017). However, the practical execution of this idealized loop is fraught with systemic challenges. Data from laboratories and radiology departments often reside in separate information silos. The scheduling of phlebotomy and imaging studies is frequently uncoordinated, leading to temporal discordance that complicates interpretation. The cognitive burden of synthesizing disparate data points falls heavily on the clinician, often without technological support. Figure 1 illustrates the iterative biomarker–imaging feedback loop underlying modern chronic disease management in oncology and autoimmune disorders.

Figure 1. The Biomarker–Imaging Feedback Loop in Oncology and Autoimmune Disease Management

This narrative review aims to map the biomarker-imaging feedback loop in the context of Internal Medicine-managed oncology and autoimmune diseases. It will synthesize literature from 2010 to 2024 to: 1) analyze the clinical evidence for integrated biomarker and imaging strategies in specific disease contexts; 2) examine the health information technology challenges and solutions for creating unified diagnostic views; 3) explore the critical, yet often overlooked, role of health assistants and care coordinators in orchestrating the logistical flow of the monitoring cycle; and 4) discuss the implications for patient-centered care and health system efficiency. By viewing the loop as a unified sociotechnical system, this review seeks to move beyond a discussion of individual tests to propose a framework for integrated diagnostic management.

Methodology

This interdisciplinary narrative review employed a systematic search strategy across biomedical and health services research databases. PubMed, Scopus, Web of Science, and CINAHL were queried for English-language articles published between January 2010 and December 2024. The search strategy utilized a combination of MeSH terms and keywords organized into conceptual clusters: (1) Diseases: "Neoplasms," "Autoimmune Diseases," "Arthritis, Rheumatoid," "Lupus Erythematosus,

Systemic"; (2) Diagnostic Modalities: "Biological Markers," "Tomography, X-Ray Computed," "Positron-Emission Tomography," "Magnetic Resonance Imaging"; (3) Clinical Process: "Disease Management," "Monitoring, Physiologic," "Treatment Outcome," "Precision Medicine"; (4) Systems: "Medical Records Systems, Computerized," "Clinical Decision Support Systems," "Patient Care Team," "Continuity of Patient Care." Boolean operators (AND, OR) were used to combine clusters, with a focus on intersections (e.g., "Biological Markers" AND "Tomography, X-Ray Computed" AND "Neoplasms").

Inclusion criteria were: peer-reviewed articles focusing on the combined or comparative use of biomarkers and imaging for diagnosis, staging, response assessment, or surveillance in solid tumor oncology or systemic autoimmune diseases; studies addressing care coordination, data integration, or workflow challenges related to multi-modal monitoring; and reviews or meta-analyses on integrated diagnostic strategies. Exclusion criteria included: studies on hematologic malignancies without solid tumor focus, articles on single diagnostic modalities without integration, and technical reports on imaging hardware or assay development without clinical correlation. The initial search yielded 602 articles. After deduplication and title/abstract screening, 88 full-text articles were assessed for eligibility, with 42 selected for in-depth synthesis. Data were extracted thematically into categories of clinical integration, technological enablement, care coordination, and system outcomes.

The Clinical Imperative in Defining the Feedback Loop in Disease Management

The biomarker-imaging feedback loop is operationalized differently but remains conceptually central in both oncology and autoimmune disease management (Viñal et al., 2022). In oncology, particularly for cancers like colorectal, lung, and prostate cancer, the loop is fundamental to assessing treatment response and detecting recurrence. Guidelines for diseases like metastatic colorectal cancer advocate for the concurrent use of CT imaging and serum tumor markers (e.g., CEA) at regular intervals during systemic therapy (Argilés et al., 2020). A discordant result—such as stable imaging but a rapidly rising CEA—presents a clinical dilemma, often prompting more sensitive imaging (like PET-CT) or a change in therapy before anatomical progression becomes evident (Cervantes et al., 2023). This scenario exemplifies the loop's predictive value, where the biomarker serves as a leading indicator (Zhang et al., 2021).

In autoimmune diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), the loop integrates inflammatory biomarkers (e.g., C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], rheumatoid factor [RF]) with imaging assessments of disease activity. The treat-to-target (T2T) strategy in RA explicitly requires the use of both clinical evaluation, biomarker levels, and increasingly, musculoskeletal ultrasound or MRI to gauge synovitis and guide therapy escalation toward remission (Smolen et al., 2020). Imaging can identify subclinical inflammation not reflected in serum markers, while biomarkers can provide a systemic inflammatory context for localized imaging findings (Chen & Chen, 2023). The feedback loop here ensures therapy is tailored not just to symptomatic relief but to the objective abatement of inflammatory disease activity, preventing long-term joint damage and disability (Colebatch et al., 2013).

The Laboratory-Radiology Nexus

The clinical utility of the feedback loop is maximized when biomarker and imaging data are temporally synchronized and interpretively synthesized. Temporal synchronization is critical; a biomarker drawn weeks after a scan loses its correlative power. Optimal practice involves scheduling blood draws and imaging studies in close temporal proximity, ideally within days, to create a coherent "snapshot" of disease status (Corso et al., 2020). However, healthcare systems rarely have built-in protocols to coordinate these appointments, leading to fragmented data that increases cognitive load and uncertainty for the clinician.

Interpretive synthesis is the cognitive task of reconciling sometimes contradictory data. Does a new, small pulmonary nodule on CT in a patient with stable CA-125 represent metastatic progression or an unrelated benign finding? Does a normal CRP in a patient with new ultrasound-proven tenosynovitis indicate a treatment failure limited to a specific anatomical site? This synthesis requires deep domain expertise and is a primary function of the managing internist or specialist, who must weigh the sensitivity, specificity, and predictive values of each modality (Guo et al., 2022). Radiologists and laboratory medicine specialists contribute by providing nuanced reports—a radiologist might comment

on the atypical appearance of a lesion in the context of a known malignancy, while a pathologist might flag a dramatically rising biomarker trend (Girard et al., 2020). The lack of a structured forum for interdisciplinary consultation on these specific patient scenarios is a significant gap in many care models (Table 1).

Table 1: The Biomarker-Imaging Feedback Loop in Clinical Practice

Disease Context	Exemplary Biomarkers	Key Imaging Modalities	Clinical Decision Triggered by Loop Data	Common Integration Challenge
Metastatic Colorectal Cancer	Carcinoembryonic Antigen (CEA), CA 19-9.	CT (chest/abdomen/pelvis), PET-CT, liver MRI.	Rising CEA with stable CT may prompt earlier scan, switch to 2nd-line therapy, or enrollment in clinical trial.	Temporal disconnect between lab draw and scan date; CEA elevation from non-malignant causes (e.g., smoking) complicating interpretation.
Prostate Cancer (on ADT)	Prostate-Specific Antigen (PSA).	CT, Bone Scan, PSMA-PET.	Rising PSA (biochemical recurrence) triggers imaging to locate disease for potential targeted radiotherapy.	Low sensitivity of conventional imaging (CT/bone scan) at low PSA levels; need for advanced PSMA-PET often limited by access/insurance.
Rheumatoid Arthritis	CRP, ESR, RF, Anti-CCP antibodies.	Musculoskeletal Ultrasound, MRI of hands/feet, conventional radiography.	Presence of power Doppler signal on ultrasound despite normal CRP may justify therapy escalation to meet treat-to-target goal.	Ultrasound is operator-dependent; biomarker levels can be normal in up to 40% of patients with active disease ("seronegative RA").
Systemic Lupus Erythematosus	Anti-dsDNA, Complement levels (C3, C4), CRP.	Renal ultrasound, Chest CT, MRI brain, Echocardiogram.	Rising anti-dsDNA with falling complement may prompt renal ultrasound or biopsy, even without new	Non-specific nature of many biomarkers; imaging findings often lag behind serological flare.

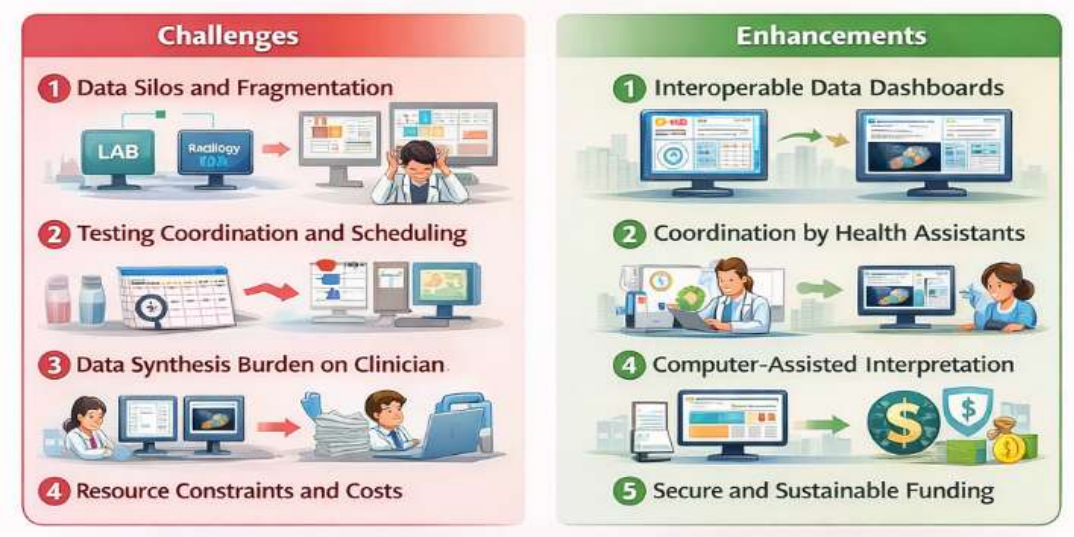
		symptoms, to detect early nephritis flare.

Health Information Technology

The electronic health record (EHR) is both the repository for and a potential barrier to an integrated feedback loop (Zhang et al., 2023). Laboratory results and radiology reports are typically stored in distinct modules, requiring clinicians to navigate multiple tabs and execute separate searches to compile a longitudinal timeline. This fragmentation impedes efficient synthesis and increases the risk of overlooking critical data (Everson et al., 2017). The solution lies in the development of integrated data dashboards or diagnostic management views.

These are specialized EHR interfaces or standalone applications that aggregate relevant data streams onto a single screen, organized chronologically (Cross et al., 2022). An oncology dashboard might display a graphical trend of PSA levels directly above a timeline of imaging reports, with hyperlinks to the actual images in the PACS (Picture Archiving and Communication System) (Perry et al., 2022). For rheumatology, a dashboard could plot CRP and ESR alongside a log of joint ultrasound findings and patient-reported outcome scores. The most advanced systems incorporate clinical decision support (CDS) rules that flag discordant patterns automatically—for example, alerting the clinician when a new CT scan report documenting "progression of metastatic disease" is finalized while the most recent CEA level, drawn the same day, shows a 50% decline (Wright et al., 2022). Creating these views requires significant health IT investment, cross-departmental collaboration between laboratory, radiology, and IT services, and a commitment to user-centered design to ensure clinician adoption (Janssen et al., 2020). Figure 2 summarizes key barriers and enabling strategies affecting the effectiveness of the biomarker–imaging feedback loop.

Figure 2. System-Level Challenges and Enhancements in the Biomarker–Imaging Feedback Loop
The Human Infrastructure



While technology aggregates data, the physical and logistical execution of the feedback loop relies on a human infrastructure often embodied by health assistants, patient navigators, or dedicated care coordinators (Tian et al., 2022). Their role is pivotal in transforming the clinical guideline into a lived reality for the patient. They are responsible for the intricate logistical coordination required: scheduling phlebotomy appointments to coincide with pre-imaging lab work (e.g., creatinine clearance for CT contrast), ensuring imaging requisitions include the correct clinical questions, coordinating prior authorization with insurers, and arranging transportation if needed (Shusted et al., 2019).

Perhaps most importantly, they act as a continuity bridge between asynchronous tests and the clinician's review. They can track when results are pending, follow up on delayed reports, and compile preliminary

data packets ahead of a clinic visit. This proactive management prevents the "missing data" scenario that breaks the feedback loop and leads to clinical inertia (Klein et al., 2023). By offloading these complex administrative tasks, health assistants enable internists to focus on the cognitive work of data synthesis and therapeutic decision-making, thereby increasing the efficiency and reliability of the entire monitoring system (Table 2).

Table 2: System Components for Optimizing the Biomarker-Imaging Feedback Loop

System Component	Current Common State	Ideal/Integrated State	Key Enablers & Required Changes
Scheduling & Logistics	Disjointed: Lab and imaging appointments made separately, often with significant lag time. Patient navigates multiple departments.	**Synchronized:** "One-stop" or tightly coordinated scheduling. Phlebotomy immediately before imaging or on same day. Pre-authorization bundled.	Implementation of integrated scheduling software; creation of "diagnostic care coordinator" roles (Health Assistants); development of clinical pathways with embedded timepoints.
Data Presentation & EHR Integration	**Siloed:** Lab results and radiology reports in separate EHR sections. Clinician must manually compile timeline.	**Unified Dashboard:** Specialty-specific views that graphically display biomarker trends alongside chronologically linked imaging reports and key images.	Health IT investment in dashboard development; adoption of interoperability standards (HL7 FHIR); collaboration between Lab, Radiology, and Informatics departments.
Interpretation & Clinical Decision Support	**Manual Synthesis:** Clinician bears full cognitive load of reconciling data. Relies on memory and manual review.	**Augmented Intelligence:** CDS rules flag discordant patterns (e.g., rising biomarker + stable scan). Platform enables easy consultation between internist, radiologist, and lab medicine.	Development and validation of context-specific CDS algorithms; creation of formal virtual tumor board or diagnostic management committees; reimbursement for inter-specialty consultation.
Patient Engagement & Communication	**Reactive/Passive:** Patient receives results piecemeal via portal or waits for clinic visit. Anxiety high during "pending" periods.	**Proactive/Supported:** Care coordinator provides a pre-visit summary. Patient portals are configured to release correlated biomarker/imaging	Design of patient-facing dashboard views; training for health assistants

	results simultaneously with clinician commentary.	in results communication and anxiety management; development of standardized patient education materials on the monitoring process.

Internal Medicine as the Integrative Discipline

The internist, or specialist internist (e.g., oncologist, rheumatologist), sits at the apex of the feedback loop as the ultimate integrator and decision-maker. This role extends beyond medical knowledge to encompass systems navigation (Olson & Burns, 2023). The internist must understand the indications, limitations, and timing of various biomarkers and imaging studies to order them judiciously. They must cultivate collaborative relationships with radiologists and laboratory medicine colleagues to resolve ambiguous cases, often through informal curbside consultations or formal multidisciplinary team meetings (Taylor et al., 2013). Furthermore, they are responsible for communicating the synthesized narrative to the patient—explaining what "stable scans but a slowly rising marker" means for prognosis and future choices, a task requiring high-level communication skills and emotional intelligence (Epstein & Street, 2011).

The internal medicine workflow must therefore be redesigned to support this integrative function. This includes protected time for reviewing complex data packages, efficient tools (like dashboards) to minimize data-gathering burden, and team-based structures that leverage the skills of health assistants and nurse practitioners to manage routine monitoring and patient communication, freeing the physician for complex synthesis and decision-making (Sinsky et al., 2020).

Future Directions and Conclusion

The biomarker-imaging feedback loop is not a futuristic concept but a present-day clinical reality whose optimization is crucial for precision medicine. Future advancements will likely focus on several key areas (Tomasik et al., 2023). First, the rise of liquid biopsy technologies—detecting circulating tumor DNA (ctDNA) in oncology—will introduce an even more dynamic and sensitive biomarker layer, creating a tighter, more real-time loop with imaging that could redefine concepts of minimal residual disease and recurrence (Ignatiadis et al., 2021). Second, artificial intelligence (AI) will play a dual role: in imaging, via automated lesion detection and quantification on CT scans, and in data synthesis, via algorithms that predict outcomes or recommend actions based on multimodal input (Bi et al., 2019). Third, patient-generated health data from wearables may enter the loop, providing functional correlates (e.g., activity levels, heart rate variability) to biochemical and anatomical data.

However, technological advancement alone is insufficient. The primary conclusion of this review is that the effectiveness of the biomarker-imaging feedback loop is fundamentally a sociotechnical challenge. It requires deliberate design of workflows, roles, and information systems. Healthcare systems must invest not only in advanced PET scanners and genomic assays but also in the health assistants who coordinate their use and the IT platforms that unify their outputs. They must create cultures of interdisciplinary collaboration that value the integrative work of the internist. By viewing the loop as an integrated system of people, processes, and technology, we can move closer to the ideal of seamless, patient-centered diagnostic management, where every test informs the next, and every data point contributes to a coherent story of health, disease, and treatment.

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حلقة التغذية الراجعة بين العلامات الحيوية والتصوير: مراجعة سردية للتشخيص المتكامل في علم الأورام والأمراض المناعية الذاتية

الملخص

الخلفية :تعتمد إدارة الأمراض المزمنة المعقدة مثل السرطان النقيلي والحالات المناعية الذاتية النظامية على التفاعل الديناميكي بين العلامات الحيوية المستمدة من المختبر والتصوير الإشعاعي. تشكل هذه العلاقة المتبادلة حلقة تغذية راجعة تشخيصية وعالجية حرجة توجه اتخاذ القرارات السريرية.
الهدف :تهدف هذه المراجعة السردية إلى تلخيص الأدلة حول الاستخدام المتكامل للعلامات الحيوية المصلية والتصوير الطبي في إدارة علم الأورام والأمراض المناعية الذاتية بقيادة الطب الباطني، مع التركيز على التنسيق النظامي المطلوب للرصد الفعال.
الطرق :تم إجراء بحث أدبي شامل في قواعد البياناتPubMed ، Scopus، Web of Science، وCINAHL (2010-2024)، مع دمج المنظورات السريرية والتكنولوجية وبحوث خدمات الرعاية الصحية.
النتائج :تحدد المراجعة أن الإدارة المثلى للمرض تعتمد على التزامن الزمني والتركيب التفسيري لبيانات العلامات الحيوية والتصوير. يعيق التكامل الناجح العزل المعلوماتي، وجداول الاختبارات غير المتزامنة، والتنسيق المجزأ. يعزز تنفيذ لوحات بيانات موحدة والنشر الاستراتيجي لمساعدي الصحة للتنسيق اللوجستي بشكل كبير من وظيفية هذه الحلقة التشخيصية.
الخاتمة :تُعد حلقة التغذية الراجعة بين العلامات الحيوية والتصوير حجر الزاوية في إدارة الأمراض المزمنة الحديثة. تتطلب فعاليتها تكاملاً متعمداً على مستوى النظام، يشمل التوافق التكنولوجي وإعادة تصميم أدوار تنسيق الرعاية.
الكلمات المفتاحية :الطب الدقيق؛ علامات الأورام؛ التصوير الطبي؛ تنسيق الرعاية؛ إدارة الأمراض المزمنة.