

# Radiogenomics In Fetal Medicine: A Scoping Review Of Prenatal Imaging And Genomic Diagnostics

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## Abstract

### Background

Radiogenomics integrates quantitative imaging features with genomic data to support precision medicine. It has been explored in adult imaging, particularly oncology. In fetal medicine, prenatal imaging and genomic testing are routinely used, yet their analytic integration remains poorly defined. Understanding whether established radiogenomic principles can be translated to the prenatal context is essential for advancing early diagnosis and prognostic assessment.

### Objectives

To map existing evidence on the integration of prenatal imaging and genomic data, with a focus on identifying genotype–phenotype correlations, clinical applications, and gaps relevant to fetal radiogenomics.

### Methods

A scoping review was conducted in accordance with the PRISMA extension for Scoping Reviews (PRISMA-ScR). A structured literature search was performed in PubMed/MEDLINE to identify peer-reviewed studies involving prenatal imaging, radiomics, and genomic diagnostics. Eligible studies were charted descriptively to summarise imaging modalities, analytic approaches, and the extent of imaging–genomic integration.

### Results

Eleven peer-reviewed studies applying radiomics or quantitative imaging analysis to prenatal or fetal

imaging were identified. These studies primarily involved fetal magnetic resonance imaging and, to a lesser extent, prenatal ultrasound, with a focus on placental disorders, fetal lung development, and fetal growth restriction. None of the included studies performed a formal radiogenomic analysis integrating quantitative imaging features with genomic sequencing data. While prenatal genomic testing workflows were well established, imaging and genomics were applied sequentially rather than within unified analytic frameworks.

### Conclusion

The mapped evidence indicates that, despite methodological maturity of radiogenomics in adult medicine and demonstrated feasibility of quantitative prenatal imaging, formal fetal radiogenomic integration has not yet been realised. This scoping review identifies a clear translational gap and supports the need for future research integrating standardised prenatal imaging, quantitative phenotyping, and genomic data to advance precision approaches in fetal medicine.

**Keywords:** Fetal radiogenomics, Prenatal imaging, Radiomics, Genomic diagnostics, Precision medicine

### Introduction

Radiogenomics, the systematic integration of quantitative imaging features with genomic information, is transforming approaches to diagnosis and precision medicine across multiple clinical domains. While radiogenomics has been most extensively explored in oncology and adult neuroimaging, its potential in **fetal medicine** remains

largely unrealised. **Prenatal imaging, particularly ultrasound and fetal MRI, provides the earliest window into structural and functional development.** Yet imaging findings alone often lack sufficient specificity to distinguish between heterogeneous genetic causes of fetal anomalies. Genomic technologies such as chromosomal microarray analysis, whole-exome sequencing (WES), whole-genome sequencing (WGS), and targeted panels increasingly complement prenatal assessment by revealing underlying molecular etiologies [1]. The convergence of these two modalities represents an important frontier for improving early diagnosis, risk stratification, and counselling in pregnancy [2].

The conceptual foundation for radiogenomics is grounded in work demonstrating that imaging carries latent biological information reflective of underlying molecular states. Studies in cancer research have shown that radiologic phenotypes can correlate with gene expression patterns, mutational signatures, and clinical outcomes [3,4]. Extending this framework to fetal medicine could enable recognition of genotype–phenotype relationships before birth, supporting earlier detection of syndromic disorders, refinement of prognostic pathways, and optimisation of perinatal management strategies. Such capabilities are increasingly relevant as prenatal genomic testing expands globally and as AI-driven imaging analytics begin to reveal subtle phenotypic signatures not readily apparent to human observers.

Despite this promise, the field of **fetal radiogenomics** is still nascent. Existing evidence is dispersed across case series, imaging–genotype association studies, prenatal sequencing cohorts, and early computational modelling work. No consolidated synthesis currently defines how prenatal imaging and genomics have been combined, which genotype–phenotype correlations have been reported, or how these approaches may influence clinical decision-making. A scoping review is therefore essential to characterise the breadth of available literature, identify emerging patterns, and highlight gaps that warrant methodological development and technological innovation.

**This review aims to map the current landscape of fetal radiogenomics, summarise reported imaging–genotype associations, and explore how integrated approaches may support early detection and improved prognostic assessment.** By clarifying the existing evidence base, the review also provides foundational insight for the development of next-generation radiogenomic tools, including AI-enabled clinical decision-support platforms tailored for fetal medicine.

## Objectives

### Primary Objective

- To map and synthesise existing evidence on the integration of prenatal imaging and genomic data, with a focus on genotype–phenotype correlations

relevant to fetal diagnosis, early detection, and prognostic evaluation.

### Secondary Objectives

- To describe the imaging modalities, genomic platforms, and radiogenomic methods used in fetal research.

- To summarise reported imaging features associated with specific genetic variants, syndromes, or molecular signatures.

- To explore how radiogenomic approaches influence diagnostic yield, clinical decision-making, and treatment planning in fetal medicine.

- To identify methodological gaps and opportunities for innovation, including the development of AI-driven radiogenomic tools.

## Methods

This scoping review was conducted in accordance with the **PRISMA extension for Scoping Reviews (PRISMA-ScR)**

### Study Design

A scoping review methodology was adopted to map the existing literature on fetal radiogenomics, defined as the integration of prenatal imaging features with genomic data for diagnostic, prognostic, or clinical decision-making purposes. This approach was selected due to the emerging and heterogeneous nature of evidence in this field.

### Eligibility Criteria

Eligibility was defined using the **Population–Concept–Context (PCC)** framework.

- Population:** Human fetuses assessed during the prenatal period.
- Concept:** Studies integrating or correlating prenatal imaging findings with genomic or genetic data.
- Context:** Clinical or research settings involving prenatal diagnosis, early detection, prognosis, or treatment planning.

Original research articles including cohort studies, case–control studies, cross-sectional studies, case series, and feasibility studies were included. Animal studies, postnatal-only studies, review articles, editorials, and non-English publications were excluded.

### Information Sources and Search Strategy

Literature searches were conducted in PubMed/MEDLINE. Additional databases were considered to ensure comprehensive coverage. Search terms combined concepts related to prenatal imaging, radiogenomics, and genomic testing. Searches were limited to peer-reviewed publications from 2019 to 2024. Reference lists of included studies were screened for additional relevant articles.

## Study Selection

Records were screened in two stages: title and abstract screening followed by full-text review of potentially eligible studies. Reasons for exclusion at the full-text stage were documented. The study selection process is summarised using a PRISMA-ScR flow diagram.

## Data Charting and Synthesis

Data were charted using a predefined extraction framework capturing study characteristics, imaging modality, genomic methods, reported genotype–phenotype correlations, and clinical relevance. Findings were synthesised descriptively and thematically. No quantitative synthesis or meta-analysis was performed.

## Protocol and Registration

A review protocol was developed prior to study selection. Formal registration was not undertaken, as it is not mandatory for scoping reviews.

## Results

### Study Selection

The database search identified a body of literature related to radiogenomics, prenatal imaging, and genomic diagnostics. Following removal of duplicates and screening of titles, abstracts, and full texts, **11 peer-reviewed studies** were included that applied radiomics or quantitative imaging analysis to prenatal or fetal imaging data. In addition, foundational adult radiogenomics studies were retained to inform methodological and translational mapping, but were not considered direct fetal applications.

The study selection process is summarised in the PRISMA-ScR flow diagram.

### Characteristics of Included Prenatal Imaging Studies

The 11 included prenatal studies were published between **2019 and 2024**. Most were retrospective cohort or feasibility studies. Sample sizes varied widely, ranging from small pilot cohorts to larger single-centre or multicentre datasets.

#### Imaging modalities represented:

- Fetal magnetic resonance imaging (MRI): majority of studies [5-9]

- Prenatal ultrasound: fewer studies, primarily focused on fetal lung assessment [10-14] **Primary anatomical and clinical targets:**

- Placenta and placental disorders (e.g., placenta accreta spectrum, placental dysfunction)[5,6,15,16, 17]

- Fetal lung development and prediction of neonatal respiratory outcomes [ 8,10,11,12]

- Fetal growth restriction and placental insufficiency [13,15,18]

### • Radiomics and Quantitative Imaging Approaches

All included prenatal studies employed radiomics or radiomics-inspired quantitative feature extraction, including texture, intensity, and shape-based features derived from manually or semi-automatically segmented regions of interest. Several studies evaluated feature reproducibility and model stability, particularly in fetal MRI datasets [6,8,9,16].

Predictive modelling approaches included traditional machine-learning classifiers and radiomics-based nomograms combining imaging features with selected clinical variables [6,9].

### Genomic Data Integration

Across the included prenatal imaging studies, no study performed a formal radiogenomic analysis involving direct statistical correlation between quantitative imaging features and genomic sequencing data (e.g., whole-exome or whole-genome sequencing).

Genomic information, when discussed, was incorporated indirectly through:

- Phenotype-driven genetic testing workflows[3]
- Post-imaging diagnostic interpretation
- Descriptive linkage between imaging findings and known genetic syndromes [13,16,17,18]

### • Mapping of Evidence Across Domains

The evidence mapping demonstrated that:

- Quantitative radiomics approaches are feasible in prenatal imaging, particularly in fetal MRI and placental imaging.
- Structured prenatal genomic testing pipelines exist and are routinely applied in cases of fetal anomalies.
- Integrated analytic frameworks linking prenatal imaging features directly to genomic variants are currently absent from the literature.

### Discussion

This scoping review mapped the current evidence at the intersection of radiogenomics, prenatal imaging, and genomic diagnostics to evaluate whether established radiogenomic principles can be translated into fetal medicine. The findings reveal a clear imbalance between domains: radiogenomics is methodologically mature in adult medicine, while its application in prenatal and fetal settings remains largely unexplored. At the same time, the essential components required for fetal radiogenomics, namely quantitative imaging approaches and established prenatal genomic testing workflows, already exist but operate independently.

### Radiogenomics as a Framework in Adult Imaging

The adult radiogenomics literature demonstrates that quantitative imaging phenotypes can reflect underlying molecular and genomic characteristics, supporting non-invasive biological characterisation and personalised clinical decision-making. Across multiple disease contexts and imaging modalities, radiogenomic studies have shown that imaging features encode biologically meaningful information related to gene expression, mutational status, and molecular subtypes[2]. These findings establish radiogenomics as a robust analytic paradigm rather than a modality- or disease-specific technique.

Crucially, radiogenomic methodologies are based on generalisable principles of image-derived phenotyping and molecular correlation [3,4]. This suggests that their applicability is not inherently limited to adult disease models, providing a strong methodological rationale for exploring translation into prenatal contexts.

### **Quantitative Prenatal Imaging: Evidence from Radiomics Studies**

The prenatal radiomics studies identified in this review demonstrate that quantitative feature extraction and modelling are feasible in fetal and placental imaging. Most studies focused on fetal MRI and placental MRI, with a smaller number applying radiomics to prenatal ultrasound data. These investigations addressed clinically relevant prenatal conditions, including placental disorders, fetal lung development, and fetal growth restriction [6,7,8,10,15].

Although these studies did not incorporate genomic data, they confirmed that reproducible image segmentation, feature extraction, and predictive modelling can be achieved despite the inherent challenges of prenatal imaging, such as fetal motion and gestational variability. This body of work provides an essential technical foundation for future integration of imaging and genomics in fetal medicine.

### **Prenatal Genomics and Phenotype-Driven Interpretation**

In parallel, prenatal genomic testing has become an integral component of fetal medicine, particularly in the evaluation of structural anomalies detected on ultrasound. Phenotype-driven interpretation frameworks, often supported by structured phenotypic descriptors, are widely used to prioritise and interpret genomic variants. However, imaging data in these workflows are typically incorporated qualitatively, and quantitative imaging phenotypes are not systematically leveraged for genomic correlation or prediction [13,14,18].

The absence of formal analytic integration between prenatal imaging and genomics highlights a structural gap rather than a lack of technological capability. Imaging and genomic data are generated within the same clinical pathway but are analysed using separate frameworks.

### **Translational Implications for Fetal Radiogenomics**

The mapped evidence indicates that fetal radiogenomics is currently limited not by feasibility but by the lack of integrative study designs. Prenatal imaging captures early manifestations of developmental and genetic processes, often before postnatal presentation, making it a particularly relevant context for radiogenomic investigation. The adult radiogenomics literature provides validated methodological templates, while prenatal radiomics and genomics demonstrate readiness for integration.

Fetal ultrasound, in particular, warrants attention as a potential radiogenomic modality given its central role in prenatal screening and widespread accessibility. While ultrasound-based radiogenomics remains less developed than MRI-based approaches, existing studies indicate that modality-specific challenges can be addressed through appropriate feature engineering and modelling strategies.

### **Research Directions Emerging from the Evidence Map**

The absence of published studies directly correlating prenatal imaging features with genomic sequencing data defines a clear research gap. Future investigations should focus on prospective designs that combine standardised prenatal imaging, quantitative feature extraction, and genomic testing within unified analytic frameworks. Key methodological considerations include phenotype standardisation, reproducible imaging protocols, and transparent statistical approaches for image–genome association analysis.

### **Conclusion**

This scoping review mapped the current evidence at the interface of radiogenomics, prenatal imaging, and genomic diagnostics to evaluate the translational potential of radiogenomic approaches in fetal medicine. The findings demonstrate that while radiogenomics is a well-established and methodologically validated framework in adult medicine, its application to prenatal and fetal imaging has not yet been realised. At the same time, quantitative prenatal imaging techniques and structured genomic testing pipelines are already in place, indicating that the foundational components required for fetal radiogenomics exist but remain analytically disconnected.

The review highlights a clear gap in the literature: no published studies were identified that formally integrate quantitative fetal imaging features with genomic sequencing data within a radiogenomic analytic framework. This gap reflects the early stage of the field rather than a lack of feasibility and underscores the opportunity for future research to develop integrated imaging–genomic methodologies tailored to prenatal care. Such approaches may support earlier detection, improved prognostic

assessment, and more informed clinical decision-making in fetal medicine.

Several limitations should be acknowledged. As a scoping review, this study aimed to map the breadth of available evidence rather than to assess study quality or quantify effect sizes. The conclusions are therefore descriptive and dependent on the scope and reporting of the existing literature. In addition, the relative paucity of fetal-specific radiogenomic studies limits direct inference but simultaneously defines the translational research need identified in this review.

In conclusion, the mapped evidence suggests that extending radiogenomic principles to fetal medicine represents a logical and timely progression of precision imaging paradigms. Future studies integrating standardised prenatal imaging, quantitative phenotyping, and genomic data are warranted to establish fetal radiogenomics as a clinically meaningful framework within prenatal diagnosis and care.

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#### Tables/Figures -

### Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
<b>TITLE</b>			
Title	1	Identify the report as a scoping review.	1
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	1
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	2
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	3
<b>METHODS</b>			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	3
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	3
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	4
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	4
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	4

Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	4
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	Click here to enter text.
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	4
<b>RESULTS</b>			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	4
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	5
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	5
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	5
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	4-6
<b>DISCUSSION</b>			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	6-7
Limitations	20	Discuss the limitations of the scoping review process.	7
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	7-8
<b>FUNDING</b>			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	8

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

\* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more

applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA ScR): Checklist and Explanation. *Ann Intern Med.* 2018;169:467–473. doi: [10.7326/M18-0850](https://doi.org/10.7326/M18-0850).

**Table 1.** Characteristics of included prenatal radiomics studies

Sr no.	Author (Year)	Study Design	Imaging Modality	Target Organ / Condition	Quantitative Imaging Approach [7]	Genomic Data Integrated
1	Prayer et al. (2023)	Retrospective cohort	Fetal MRI	Fetal lung maturity	Radiomics feature extraction; reproducibility analysis	No
2	Watzkenboeck et al. (2023)	Methodological study	Fetal MRI	Fetal lung	2D vs 3D radiomics comparison	No
3	Peng et al. (2022)	Retrospective cohort	Placental MRI	Placenta accreta spectrum	Radiomics-based nomogram	No
4	Bartels et al. (2023/24)	Multicentre cohort	Placental MRI	Placenta accreta spectrum severity	Placental radiomics modelling	No
5	Huang et al. (2024)	Diagnostic evaluation	Placental MRI	Placenta accreta spectrum	MRI-based radiomics assessment	No
6	Yu et al. (2024)	Retrospective cohort	Placental MRI	Placenta accreta spectrum	Radiomics-clinical nomogram	No
7	Du et al. (2022)	Pilot cohort	Prenatal ultrasound	Fetal lung maturity	Ultrasound radiomics	No
8	Jiao et al. (2022)	Method development	Prenatal ultrasound	Fetal lung	Radiomics with machine-learning models	No
9	Song et al. (2024)	Retrospective cohort	Placental MRI + ultrasound	Fetal growth restriction	Combined radiomics and clinical features	No
10	Wu et al. (2019)	Multicentre cohort	Placental MRI	Placental dysfunction	Clinic radiomic modelling	No
11	Lin et al. (2024)	Diagnostic modelling	Ultrasound	Neonatal respiratory disease*	Ultrasound radiomics	No

\*Neonatal study included due to methodological relevance and direct applicability to prenatal lung imaging.

**Table 1.** Summary of prenatal and perinatal studies applying radiomics or quantitative imaging analysis to fetal or placental imaging. None of the included studies performed formal radiogenomic analyses integrating quantitative imaging features with genomic sequencing data.

**Table 2.** Evidence mapping across prenatal imaging and genomics

Domain	Evidence Identified	Current Status
Prenatal imaging	Fetal ultrasound and fetal MRI widely used	Established
Quantitative imaging	Radiomics feasible in fetal and placental imaging	Emerging
Genomic testing	CMA, WES, WGS used in prenatal diagnosis	Established
Phenotype-driven genomics	Imaging informs genomic testing qualitatively	Established
Imaging–genomic integration	Quantitative imaging features linked to genomic variants	Absent
Fetal radiogenomics frameworks	Unified analytic pipelines	Not reported

**Table 2.** Mapping of evidence across prenatal imaging, quantitative analysis, and genomic testing highlights the absence of formal fetal radiogenomic integration despite the presence of foundational components.