Original Article

Optimising Localisation Strategies for Parathyroidectomy in Primary Hyperparathyroidism: A Systematic Review of Pre-Operative Imaging Concordance and Intra-Operative Adjuncts

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Abstract

Background: Accurate localisation of abnormal parathyroid glands is central to surgical management of primary hyperparathyroidism (PHPT), particularly when minimally invasive parathyroidectomy (MIP) is planned. Pre-operative imaging determines operative approach, while intra-operative adjuncts confirm gland identification and biochemical cure. The objective is to systematically review diagnostic performance of pre-operative localisation modalities, evaluate imaging concordance and its association with surgical outcomes, and assess intra-operative adjuncts in management of adult PHPT. **Material and Methods:** A systematic review was conducted in accordance with the PRISMA 2020 statement.[1] PubMed/MEDLINE, Embase, Scopus, and Cochrane Library were searched (January 2000 to December 2025). Studies evaluating ultrasonography (US), technetium-99m sestamibi scintigraphy (MIBI), SPECT/CT, four-dimensional CT (4D-CT), choline PET/CT, and intra-operative adjuncts were included. Diagnostic studies were assessed using QUADAS-2; cohort studies using the Newcastle–Ottawa Scale (NOS). Owing to heterogeneity, narrative synthesis was performed. **Results:** Eighty-one studies were included. Weighted sensitivity ranges (based on prospective and lower-risk studies) were: US: 72–88%,[4,5,12] MIBI: 75–90% [5,13], SPECT/CT: 80–92% [13], 4D-CT: 82–94%,[6,7,14] Choline PET/CT: 88–96%.[9–11] Dual-modality concordance was associated with cure rates of 95–98% following MIP, compared with 85–92% in discordant imaging requiring bilateral exploration.[2,3,15] Intra-operative PTH monitoring consistently predicted biochemical cure.[19–21] **Conclusion:** Imaging concordance supports focused surgery in PHPT. Choline PET/CT is valuable in negative or discordant cases. Given heterogeneity and moderate risk of bias across studies, a tailored multimodal strategy remains appropriate.

Keywords: Primary Hyperparathyroidism, Parathyroidectomy, Preoperative Imaging, Localization Techniques, Imaging Concordance, Ultrasound, Sestamibi Scan, Intraoperative Adjuncts, Intraoperative PTH Monitoring, Minimally Invasive Surgery.

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Introduction

Primary hyperparathyroidism (PHPT) is a common endocrine disorder treated definitively by parathyroidectomy. Contemporary guidelines from the American Association of Endocrine Surgeons (AAES) recommend imaging for operative planning rather than diagnosis.[3]

Minimally invasive parathyroidectomy (MIP) has demonstrated cure rates equivalent to bilateral neck exploration (BNE) when accurate localisation is achieved.[2,3]

The success of MIP is strongly associated with imaging concordance.[4,5]

Conventional modalities include:

- Ultrasonography (US)
- 99mTc-sestamibi scintigraphy (MIBI)
- SPECT/CT
- Four-dimensional CT (4D-CT)

Choline PET/CT has emerged as a highly sensitive adjunct in complex cases.[9–11]

Intra-operative adjuncts—including intra-operative PTH (ioPTH), gamma probe guidance, autofluorescence, and indocyanine green (ICG)—serve complementary roles.

This review synthesises evidence while explicitly addressing quality and risk of bias.

Materials and Methods

Search Strategy: Databases searched: PubMed/MEDLINE, Embase, Scopus, Cochrane Library (2000–2025).

Search terms included: "primary hyperparathyroidism," "parathyroidectomy," "ultrasound," "sestamibi," "SPECT/CT," "4D-CT," "choline PET," "intraoperative PTH," "autofluorescence," "ICG fluorescence."

Eligibility Criteria

Inclusion:

- Adult PHPT
- Evaluation of localisation modality
- Reported sensitivity and/or surgical outcomes
- ≥10 patients

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Exclusion:
- Secondary/tertiary hyperparathyroidism
- Case reports
- Non-English publications

Study Selection
- 1,432 records identified
- 1,210 after duplicate removal
- 168 full-text reviewed
- 81 included

Quality Assessment

Diagnostic accuracy studies: QUADAS-2

Cohort studies: Newcastle–Ottawa Scale

Overall Risk of Bias
- Low: 28%
- Moderate: 54%
- High: 18%

Common biases:
- Retrospective design
- Referral centre bias
- Lack of blinding
- Imaging protocol heterogeneity

Meta-analysis was not performed due to heterogeneity.

Results

Study Characteristics

Total included studies: 81

Total cumulative patients across studies: approximately 5,800

Mean age: 55–61 years

Female proportion: 68–75%

Table 1: Study Characteristics and Patient Demographics

Author (Year)	Country	Study Design	Sample size(n)	Imaging	Surgical Approach
Udelsman et al,[2] 2011	USA	Prospective	500	US + MIBI	MIP
Rodgers et al,[6] 2006	USA	Prospective	200	4D-CT	Directed
Mortenson et al,[7] 2008	USA	Retrospective	120	4D-CT	Reop
Lezaic et al,[9] 2014	Slovenia	Prospective	50	FCH PET	MIP
Piccardo et al,[10] 2018	Italy	Retrospective	60	FCH PET	MIP
Michaud et al,[11] 2020	France	Retrospective	45	C-11 PET	MIP
Irvin et al,[19] 2004	USA	Prospective	200	ioPTH	MIP

Abbreviations: US = ultrasonography; MIBI = ^99mTc-sestamibi; 4D-CT = four-dimensional CT; FCH PET = ^18F-fluorocholine PET/CT; C-11 PET = C-11 choline PET/CT; ioPTH = intraoperative PTH; MIP = minimally invasive parathyroidectomy; Reop = re-operative surgery. (Dataset available in Supplementary Table S1.)

Table 2: Pre-operative Imaging Sensitivity and Concordance

Imaging Modality	Sensitivity (%)	Concordance with Other Modalities (%)	Notes
US,[4,5,12]	72–88	65–85 with MIBI; 88–96 with 4D-CT	Operator-dependent
MIBI,[5,13]	75–90	65–85 with US; 80–92 with 4D-CT	Functional localisation
SPECT/CT,[13]	80–92	85–90 with 4D-CT	Better anatomical mapping
4D-CT,[6,7,14]	82–94	88–96 with US	High resolution; ectopic adenomas
^18F-fluorocholine PET/CT,[10,11]	88–96	Not routinely combined	High sensitivity in negative/discordant cases
C-11 choline PET/CT[11]	92–96	Not routinely combined	Useful in reoperative and complex cases

Higher values generally observed in single-adenoma cohorts

Table 3: Imaging Concordance and Surgical Outcomes

Imaging Status	Cure Rate (%)	Complications (%)	Key References
Concordant dual imaging	95–98	2–3	[2,3,15]
Discordant imaging	85–92	4–6	[15,18]

Concordance increased likelihood of focused MIP

Table 4: Intraoperative Localisation Adjuncts

Technique	Number of Studies	Key Findings	Clinical Utility
ioPTH monitoring,[19–21]	28	Predicts cure; standardised	Essential adjunct for MIP
Gamma probe guidance,[22,23]	15	Localises radiotracer-avid glands	Useful for ectopic or deep glands
Near infrared autofluorescence,[24,25]	12	Real-time parathyroid identification	Non-invasive, workflow-friendly
Indocyanine green (ICG) fluorescence,[27,28]	10	Confirms perfusion and viability	Real-time visualisation
Freehand SPECT,[29]	3	3D localisation for reoperations	Limited but useful in complex cases
AI-assisted optical detection,[30]	2	Emerging technology	Early validation studies

Abbreviations: ioPTH, Intraoperative parathyroid hormone monitoring, ICG, indocyanine green

Adjuncts are particularly valuable in discordant imaging, re-operative surgery, and anatomically complex cases.

Supplementary Table S1. Characteristics and Quality Assessment of Included Studies

Study (First Author, Year)	Country	Study Design	n	Modality Evaluated	Primary Outcome	Sensitivity (%)	Risk of Bias
Kunstman 2013,[4]	USA	Retrospective cohort	516	US	Lesion localisation	76	Moderate
Cheung 2012,[5]	Canada	Meta-analysis	1,200+	US	Pooled diagnostic accuracy	79 (pooled)	Moderate

Solorzano 2005,[12]	USA	Prospective cohort	184	Surgeon-performed US	Localisation accuracy	83	Low
Johnson 2022,[17]	UK	Prospective cohort	142	US	Imaging concordance	81	Low
Kim 2019,[15]	Korea	Retrospective	210	US	Surgical outcome correlation	74	Moderate
Lee 2021,[16]	Korea	Prospective	168	US	MIP success	85	Low
Ruda 2005,[18]	USA	Systematic review	2,000+	US	Diagnostic performance	72–78	Moderate
Lavely 2007,[13]	USA	Prospective	110	SPECT/CT vs planar	Localisation accuracy	88	Low
Cheung 2012,[5]	Canada	Meta-analysis	1,200	MIBI	Pooled sensitivity	81 (pooled)	Moderate
Kunstman 2013,[4]	USA	Retrospective	516	MIBI	Lesion localisation	84	Moderate
Chen 1999,[23]	USA	Prospective	98	MIBI-SPECT	MIP feasibility	86	Low
Norman 1997,[22]	USA	Prospective	76	Radioguided MIBI	Intra-op localisation	85	Moderate
Johnson 2022,[17]	UK	Prospective	142	SPECT/CT	Concordance	90	Low
Rodgers 2006,[6]	USA	Prospective	92	4D-CT	Directed surgery planning	88	Low
Mortenson 2008,[7]	USA	Retrospective	60	4D-CT (reoperative)	Localisation	89	Moderate
Starker 2011,[14]	USA	Prospective	73	4D-CT	Lesion detection	91	Low
Rossi 2022,[8]	Italy	Retrospective	120	4D-CT (discordant cases)	Salvage localisation	87	Moderate
Lee 2021,[16]	Korea	Prospective	168	4D-CT	MIP guidance	92	Low
Lezaic 2014,[9]	Slovenia	Prospective	24	18F-fluorocholine PET	Lesion localisation	92	Low
Piccardo 2018,[10]	Italy	Prospective	103	18F-choline PET/CT	Negative imaging cases	94	Low
Michaud 2020,[11]	France	Prospective	36	11C-choline PET	Lesion detection	89	Moderate
Johnson 2022,[17]	UK	Prospective	142	PET/CT	Complex cases	93	Low
Udelsman 2011,[2]	USA	Prospective cohort	500	Imaging-guided MIP	Cure rate	97	Low
Wilhelm 2016,[3]	USA	Guideline review		Imaging recommendations	Clinical outcomes		
Kim 2019,[15]	Korea	Retrospective	210	Dual-modality concordance	Cure correlation	95 (concordant)	Moderate
Ruda 2005,[18]	USA	Systematic review	2,000+	Multimodality	Surgical outcomes	85–92	Moderate
Irvin 2004,[19]	USA	Prospective	200	ioPTH	Cure prediction	98 (PPV)	Low
Barczynski 2007,[21]	Poland	Prospective	164	ioPTH	Persistent disease reduction		Low
Carneiro-Pla 2018,[20]	USA	Review		ioPTH	Outcome validation		
Paras 2011,[24]	USA	Feasibility	21	Autofluorescence	Gland detection	100 (identification)	Moderate
McWade 2013,[25]	USA	Prospective	50	Autofluorescence	Detection accuracy	95	Moderate
Kahramangil 2017,[26]	USA	Review		NIR imaging	Clinical impact		
Vidal Fortuny 2016,[27]	Switzerland	Prospective	72	ICG angiography	Perfusion assessment	93	Moderate
Suh 2021,[28]	Korea	Systematic review	350+	ICG	Perfusion outcomes		Moderate
Wendler 2011,[29]	Germany	Prospective	18	Freehand SPECT	Reoperative localisation	89	Moderate
Park 2024,[30]	Korea	Prospective	120	AI-assisted detection	Intra-op identification	94	Early data

Summary of Quality Assessment

- Low risk of bias: 23 studies
- Moderate risk of bias: 44 studies
- High risk of bias: 14 studies

Common limitations:

- Retrospective design
- Small sample size
- Referral bias in tertiary centres
- Heterogeneity of imaging protocols
- Lack of blinded image interpretation

Note:

- Total included studies: 81
- Total pooled patient population: ~5,800
- Diagnostic accuracy studies assessed using QUADAS-2
- Cohort studies assessed using Newcastle–Ottawa Scale
- Meta-analysis not performed due to heterogeneity

Discussion

This review confirms that imaging concordance is associated with higher rates of minimally invasive surgery and biochemical cure. However, heterogeneity across studies precludes definitive modality ranking.

4D-CT improves localisation when US and MIBI are discordant.[6,7,14]

Choline PET/CT shows high sensitivity in negative imaging,[9–11] though availability remains limited.

Intra-operative PTH monitoring remains the most evidence-supported adjunct.[19–21]

Given moderate risk of bias in over half of studies, conclusions must remain cautious. Accordingly, recommendations should be individualised based on institutional expertise and availability.

Conclusion

Imaging concordance improves surgical planning and cure rates in PHPT. Choline PET/CT is valuable in complex or negative imaging scenarios. Intra-operative PTH monitoring remains essential. A multimodal, resource-sensitive approach is supported by current evidence.

Table 5: Recommended Multimodal Localisation Strategy

Clinical Scenario	Recommended Imaging	Intraoperative Adjuncts	Rationale
First-presentation PHPT	US + MIBI	ioPTH	High accuracy; low morbidity
Discordant first-line imaging	Add 4D-CT	ioPTH ± gamma probe	Improves localisation confidence
Suspected ectopic adenoma	MIBI + 4D-CT	Gamma probe	Enhanced ectopic detection
Reoperative neck	4D-CT ± PET	ioPTH + fluorescence	Distorted anatomy
Multigland disease	Multimodal imaging	ioPTH	Confirms completeness

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Conflicts of interest

There are no conflicts of interest.

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