The use of telecytology for the evaluation of thyroid nodules fine-needle aspiration biopsy specimens: a systematic review

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Vittorio Oteri MD[1*], Simone Piane MD[2], Elisa Cocci MD[3]

[1]Endocrine Unit, Department of Clinical and Experimental Medicine, University of Catania, Garibaldi-Nesima Hospital, Catania, Italy

[2]Department of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy

[3]Department of Clinical and Experimental Medicine, Marche Polytechnic University, Ancona, Italy

**Correspondence should be addressed:*

Vittorio Oteri, Endocrine Unit, Department of Clinical and Experimental Medicine, University of Catania, Garibaldi-Nesima Hospital, Catania, Italy; email: research@droteri.it

Appendix 1. *Search strategy*

PubMed search strategy:

(((telemedicine OR "Telemedicine"[Mesh] OR Telehealth OR Teleconsultation OR eHealth OR (digital health)) AND (cytology OR cytopathology OR "Cytology"[Mesh])) OR telecytology OR telecytopathology OR Telepathology OR "Telepathology"[Mesh] OR (virtual microscopy) OR (virtual cytology) OR cytotechnology OR (digital image)) AND (Thyroid OR "Thyroid Gland"[Mesh]) AND ((Fine-Needle Aspiration) OR (Biopsy, Fine-Needle) OR (Aspiration Biopsy) OR "Biopsy, Fine-Needle"[Mesh] OR FNAB OR FNA)

Embase and Cochrane Library search strategy:

(((telemedicine OR Telehealth OR Teleconsultation OR eHealth OR (digital health)) AND (cytology OR cytopathology)) OR telecytology OR telecytopathology OR Telepathology OR (virtual microscopy) OR (virtual cytology) OR cytotechnology OR (digital image)) AND (Thyroid) AND ((Fine-Needle Aspiration) OR (Biopsy, Fine-Needle) OR (Aspiration Biopsy) OR FNAB OR FNA)

Table 1S. *Risk of bias assessment of the included non-randomized studies following the ROBINS-I tool*

Author et al. (Year)	Confounding	Selection of participants into the study	Classification of interventions	Deviations from intended interventions	Missing data	Measurement of the outcome	Selection of the reported result	Overall
Archondakis et al (2009)	Low	Low	Low	Moderate	Low	Low	Low	**Moderate**
Archondakis et al (2021)	Low	Low	Low	Moderate	Low	Low	Low	**Moderate**
Canberk at al (2019)	Low	Low	Low	Low	Low	Low	Low	**Low**
Costa et al (2018)	Moderate	Low	Low	Low	Low	Low	Low	**Moderate**
Georgoulakis et al. (2010)	Low	Low	Low	Low	Low	Low	Low	**Low**
Gerhard et al (2013)	Moderate	Low	Low	Moderate	Moderate	Moderate	Low	**Moderate**
Izquierdo et al. (2013)	Low	Low	Low	Moderate	Moderate	Low	Low	**Moderate**
Khurana et al (2011)	Low	Low	Low	Moderate	Low	Low	Moderate	**Moderate**
Lin et al. (2020)	Low	Low	Low	Low	Low	Low	Low	**Low**
Mosquera-Zamudio et al. (2019)	Moderate	Moderate	Low	Low	Moderate	Moderate	Moderate	**Moderate**
Sahin et al (2018)	Moderate	Moderate	Low	Low	Low	Low	Low	**Moderate**
Trabzonlu et al. (2022)	Moderate	Low	Moderate	Low	Serious	Low	Moderate	**Serious**
Yao et al. (2018)	Moderate	Low	Low	Moderate	Moderate	Low	Low	**Moderate**

Table 2S. *Quality assessment of the outcomes following GRADE approach*

Outcome	Study design	Risk of Bias	Inconsistency of results	Indirectness of evidence	Imprecision	Publication bias	Large magnitude of effect	Dose-response gradient	Plausible confounding	Quality
Diagnostic concordance between diagnosis via telecytology and conventional cytology	Observational	Unclear	Undetected	Undetected	Undetected	Undetected	N/A	N/A	No	**Moderate**
Preliminary assessment of adequacy of samples	Observational	Unclear	Undetected	Undetected	Undetected	Undetected	N/A	N/A	No	**Moderate**
Evaluation of telecytology image quality	Observational	Low	Undetected	Undetected	Undetected	Undetected	N/A	N/A	No	**High**

N/A – Not applicable;

Table 3S. *Characteristics of the included studies*

Author et al. (Year)	Country	Type of study	Number of thyroid cases	Telecytology technique	Main Findings
Archondakis et al. (2009)	Greece	Retrospective	252	Static images	Concordance rate between TC and CC had a k=0.94. Diagnostic accuracy of TC and CC compared with Histology diagnosis was similar (always above 96.69%). Image quality was really good in more than 80% of cases.
Archondakis et al. (2021)	Greece	Retrospective	141	Static images	Concordance rate between the 3 cytopathologist for benign and malignant lesions had k=0.85, k=0.84 and k=0.88, and for indeterminate lesions k=0.73 and k=0.78. Interobserver reproducibility between TC and Histology had a k=0.75. Image quality was nearly perfect or perfect for most of the images.
Canberk et al. (2020)	Turkey	-validation phase Retrospective -study phase Prospective	validation phase: 25 study phase: 227	Virtual slide WSI	Adequacy agreement between TC and CC was 88% in the validation phase. Diagnostic accuracy compared with Histology ranged from 80% to 100%, dependending on diagnostic cathegories in the study phase.
Costa et al. (2018)	Brazil	Prospective	42	Real-time mycroscopy with a smartphone	Adequacy agreement between TC and CC was 90.5% (k=0.461). Diagnostic agreement between TC and CC was 83.3% (k=0.685). Transmission quality was excellent or good in the majority of cases, poor in 19%. The quality influenced agreement rate: Low quality k=0.5, good k=0.625, excellent k=0.774.
Georgoulakis et al. (2011)	Greece	Retrospective	270	Static images	Interobserver agreement between TC and the initial CC was very high in all the rounds (k =0,921-0,955). Interobserver agreement in the initial rounds and in the reviews was nearly perfect and improved over the course of the review rounds (k = 0,870-0,939). Intraobserver agreement (between the checking and the review rounds) ranged within k =0,967-1 depending on the pathologist's experience.
Gerhard et al. (2013)	Portugal	Retrospective	222	Virtual slide WSI	Intraobserver agreement between TC and CC was 77.5%, with k=0.54, with more non-diagnostic cases in TC (20.3% vs 8.1%); concordance rate for malignant and benign lesions was high (75% and 83.3%). Interobserver concordance rate was 80.2% with k=0.57, it was 0.0% for indeterminate lesions, and 93.3% and 100% respectively for benign and malignant lesions
Izquierdo et al. (2013)	USA	Retrospective	92	Real-time mycroscopy	Concordance rate between TC preliminary diagnosis and the CC was excellent for benign and malignant cases in the transmitted group, the only discrepancies were in the unsatisfactory group.
Khurana et al. (2011)	USA	Retrospective	100	Real-time mycroscopy	Accuracy rate between TC and CC was 94%. Unsatisfactory rate with TC was 21%, reduced to 17% in final cytologic evaluation.
Lin et al. (2020)	USA	Retrospective	2387	Real-time mycroscopy	Unsatisfactory rate in the study group after the introduction of ROSE and TC ROSE lowered significantly. In the control group it remained unchanged. Adequacy assessment agreement between remote ROSE and final adequacy assessments was 97% (242/250) and k= 0.699.
Mosquera-Zamudio et al. (2019)	Colombia	Retrospective	10 (65% of total cases)	Virtual slide WSI	Concordance rate between the TC and CC ranged between 36 and 71%, Interobserver agreement was 93% for malignant cases, 79% for benign, and 64% for indeterminate. Overall interobserver agreement was poor (k= 0.152, P< 0.0001). Image quality scores were 8.3 for Hamamatsu WSI and 8.7 for Panoptiq slides.
Sahin et al. (2018)	Turkey	Retrospective	52 (30% of total cases)	Static-images with a smarthphone	Concordance rate between TC and CC was 78.85% (k=0.839). Patient management changed with TC diagnosis in 15.38% of cases
Trabzonlu et al. (2022)	USA	Retrospective	20 (38% of total cases)	Real-time microscopy	Adequacy concordance rate in the first case set was 83.3%. In the second case set the adequacy concordance rate was 94.8%, the diagnostic category concordance was 91.9%, the specific diagnosis concordance was 88.1%.
Yao et al. (2018)	USA	Retrospective	16 (27% of total cases)	Real-time microscopy; Virtual slide SZDS	For adequacy assessment the interobserver agreement was higher for CLM and SZDS (k = 0.74). The intermodality agreement was k=0.94 and 1 for cytopathologist A (CLM vs VDM and CLM vs SZDS) and 0.74 and 0.86 for Cytopathologist B. For preliminary diagnosis the interobserver agreement was higher for SZDS (k=0.70). The intermodality agreement was k=0.85 and 0.93 for Cytopathologist A and 0.7 and 0.75 for Cytopathologist B.

CC - Conventional Cytology; CLM - Conventional Light Microscopy; ROSE - Rapid On Site Evaluation; SZDS - Single Z-stack Digital Scan; TC – Telecytology; VDM - VisionTek Digital Microscope; WSI - Whole Slide Imaging.