

Automated paraffin embedding of tissue samples significantly reduces overall workflow time in routine pathology practice

Alessandro Gambella^{1,2}, Laura Zito², Cristina Bottaro², Michele Paudice^{1,2}, Giulia Tacchino², Viviana Accorrà², Claudio Piccione², Martina Terrile², Anna Silvana Bevere², Barbara Massa², Silvia Bozzano^{1,2}, Federica Grillo^{1,2*}, Luca Mastracci^{1,2}

¹ Unit of Pathology, Department of Surgical Sciences and Integrated Diagnostics (DISC), University of Genoa, Genoa, Italy; ² Academic Unit of Pathology (U77) - IRCCS Azienda Ospedaliera Metropolitana (AOM) San Martino Policlinic Hospital, Genoa, Italy

Summary

Objective. Automated paraffin embedding (AE) offers a solution to the operator-dependent variability and time demands manual embedding (ME), but comparative data are limited.

Methods. We quantitatively assessed AE versus ME using 186 endoscopic biopsies, 106 needle biopsies, and 62 transurethral resections, recording the time (seconds, s) required for preparation, embedding, trimming, and sectioning.

Results. AE substantially reduced embedding time (5 s for all sample types) compared with ME (43 s for endoscopic biopsies, 66.5 s for needle biopsies, and 105 s for transurethral samples), and it allowed laboratory technicians to perform other tasks concurrently. AE also shortened total time: 150.2 s (AE) vs. 250.4 s (ME) for endoscopic biopsies, 176.9 s (AE) vs. 324.2 s (ME) for needle biopsies, and 149.5 s (AE) vs. 335 s (ME) for transurethral resections.

Conclusions. These real-world data provide quantitative evidence of AE-related time savings in daily routine activity, supporting its role in workflow automation and standardization in pathology units.

Key words: automated embedding, workflow optimization, histopathology automation

Introduction

Tissue sample preparation and analysis in pathology units have historically been considered as a “workshop art”¹, owing to their close resemblance to painting and art practices (e.g., shared nomenclature and reagents, working with colors and patterns), and the use of protocols that, similar to artisanal formulas, adapt to specific expertise and environmental conditions (e.g., water hardness and air moisture). More recently, pathology units have progressively implemented automated and digitized processes, thus transitioning from a “workshop art” to a “chain of automation.” This innovation has been driven by technicians and pathologists workforce shortage, advances in laboratory equipment and software, and the growing need for standardized and reproducible procedures. Indeed, the reliability of histopathological diagnosis depends not only on pathologists interpretative expertise, but also on the accuracy and consistency of pre-analytical processes². Among these, paraffin embedding represents a critical step, ensuring that tissue samples are adequately supported and properly oriented for pathologist evaluation.

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Correspondence

Federica Grillo
federica.grillo@unige.it

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Although reliable, manual embedding (ME) performed by trained technicians remains operator-dependent, time-consuming, and prone to human error. Orientation variability is particularly critical when multiple biopsy fragments must be aligned within the same cassette on a single geometrical plane, as misaligned fragments may cause false negative results if not properly exposed during sectioning. Recent technological advances have led to automated embedding (AE) systems designed to standardizing the process, reducing technician workload, and improving reproducibility. AE also ensures consistent tissue orientation by levelling tissue geometry and z-plans, while minimizing manual manipulation of samples and integrating tracking systems, thus further reducing the risk of human error^{3,4}.

Despite these advantages, systematic data on the impact of AE on laboratory workflow remain scarce. To the best of our knowledge, no study has quantitatively compared the time requirements of ME versus AE under routine diagnostic conditions. In this study, we aimed to address this gap by analyzing a large series of biopsies and comparing the times spent by technicians during ME and AE across all procedural phases.

Materials and methods

SAMPLE COHORT

This study was performed at the Academic Pathology Unit of the IRCCS San Martino Hospital/University of Genoa, as part of our research line in quality control and workflow optimization in pathology⁵⁻¹¹. Considering the major impact of the embedding step on biopsies compared to surgical samples, only biopsies were collected. As the pathology unit had no control over the nature or origin of submitted samples, no selection criteria based on tissue type (e.g., organ of origin) were applied. To avoid disrupting routine diagnostic activity, data collection was performed one day per month over a six-month period (May-September 2023). A total of 354 routine biopsies were included [186 endoscopic biopsies, 106 needle biopsies, and 62 transurethral prostate (TURP)/bladder (TURB) specimens], formalin-fixed, processed following standard procedures^{6,8}, and then randomly assigned to either ME or AE (Tab. I).

For ME (Leica EG1150; Leica Biosystems, Deer Park, IL, USA), tissue fragments were oriented within stainless steel molds, filled with liquid paraffin, and cooled on a refrigerated plate.

For AE (Tissue-Tek AutoTEC® a120 system; Sakura

Table I. Sample distribution across ME and AE.

Sample type	Overall	ME, exact number (percentage)	AE, exact number (percentage)
Endoscopic biopsies	186	88 (47.3%)	98 (52.7%)
Needle biopsies	106	59 (55.7%)	47 (44.3%)
TURB and TURP	62	12 (19.3%)	50 (80.6%)
Total	354	159 (44.9%)	195 (55.1%)

Finetek, Torrance, CA, USA), specimens were loaded into Paraform® cassettes using different formats depending on the size of the samples: standard (28x20 mm), normal biopsy (26x19 mm), and small biopsy (13x13 mm).

For all cases, the following time points were recorded:

- **Preparation time:** time required to insert samples into the cassette and prepare them for embedding.
- **Embedding time:** duration of ME vs. AE.
- **Trimming time:** grossing of the paraffin prior to sectioning.
- **Sectioning time.**

Times were collected independently for each cassette. Time recording has been performed by a technician that shadowed the routine daily activity of their colleagues during described phases. Time was recorded with a standard stopwatch. All procedures were performed by technicians with dedicated training and long-standing experience for daily routine pathology unit sample management, according to routine shifts. Only the time spent by technicians for each procedure was recorded, rather than the duration of the total phase. Accordingly, AE embedding time was standardized at 5 s: this is not the time spent by the automatic embedder to complete the procedure (which is about 40 s), but rather the time used by the technicians to load the cassettes into the machine. Similarly, ME embedding phase was supplemented with tissue cassette cooling and scraping time, which was standardized to 120 s per cassette.

STATISTICAL ANALYSIS AND ETHICAL COMMITTEE

Statistical analysis was performed with R/RStudio software (versions 4.4.3 and 2024.12.1+563). Data were reported as median, and differences between AE and ME were compared using the t-student test. A p-value < 0.05 was considered statistically significant. The study was conducted in accordance with the Declaration of Helsinki (1964) and its subsequent amendments. Written informed consent was waived, as the

study involved no interventions impacting patient care.

Results

ENDOSCOPIC BIOPSIES

A total of 186 endoscopic biopsies were analyzed and subgrouped into 88 ME and 98 AE. Cases were stratified by the number of fragments due to its substantial impact on embedding time (Tab. II).

For preparation, the median time for one fragment was higher than that for two or more fragments; cases with 5-6 fragments also showed increased preparation times. For embedding, a marked difference was observed between AE and ME, both in the technician's active embedding time (43 s for ME vs. 5 s for AE), and, more remarkably, when considering

additional procedural-specific steps (ME: +120 s for cassette cooling and scraping; AE: +40 s for the complete embedding phase). Trimming time increased with the number of fragments for both methods, and, notably, AE trimming time (19.2 s) was longer than ME (12.7 s). Similarly, sectioning times were slightly shorter for ME (39.5 s) compared to AE (41.5 s).

Comparison between ME and AE was performed using the raw timing data (without considering the number of fragments). Statistically significant differences were observed for all phases, with preparation, trimming, and sectioning being shorter for ME ($p = 0.002$, $p < 0.001$, and $p < 0.001$, respectively), whereas embedding was shorter for AE ($p = 0.001$). Despite these results, the gain of time obtained in the AE embedding phase alone was superior to the sum of all the ME-related gain of times (preparation, trim-

Table II. Details of ME and AE timing for the endoscopic biopsy subgroup.

Characteristics	Number of fragments									
	1	2	3	4	5	6	8	9	Overall	p
ME, n (%)	21 (24)	41 (47)	14 (16)	9 (10)	2 (2)	1 (1)	0	0	88 (100)	n.a.
AE, n (%)	24 (25)	55 (56)	8 (8)	3 (3)	5 (5)	1 (1)	1 (1)	1 (1)	98 (100)	
Preparation time (median)										
ME, s	36	34	34.5	37	33	59	n.a.	n.a.	35.2	0.002
AE, s	45	40	36	39	98	44	132	117	44.5	
Embedding time (median)										
ME, s	46.5	35	37.5	40	46	48	n.a.	n.a.	43 (+120)*	0.001
AE, s	5	5	5	5	5	5	5	5	5 (+40 [§])	
Trimming time (median)										
ME, s	12	12	12.5	13	25.5	18	n.a.	n.a.	12.7	< 0.001
AE, s	19.5	19	19	13	14	20	20	20	19.2	
Sectioning time (median)										
ME, s	40	39	38.5	44	43	37	n.a.	n.a.	39.5	< 0.001
AE, s	43	44	39	40	46	46	40	38	41.5	

*: supplement to adjust for cooling and scraping time of the cassette required for ME only; §: supplement if considering the whole AE procedure rather than the sole technician time; °: t-student test.

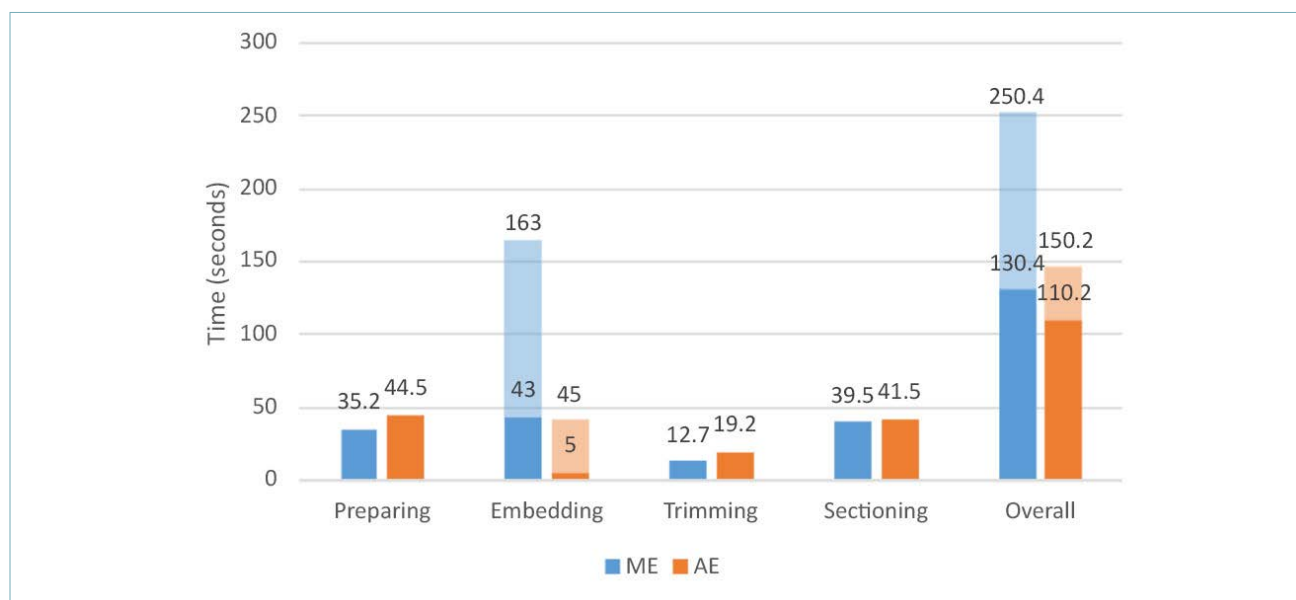


Figure 1. Graphic representation of the specific phases and overall timing for ME and AE for the endoscopic biopsy subgroup. Solid histograms represent the time spent by technicians on the specific phase. Shaded histograms in the embedding phase and overall time represent the supplement time requested if considering cooling and scraping (+120 s) with the ME approach, and the procedure as a whole (+40 s) rather than the technician time with the AE approach.

Table III. Details of ME and AE timing for the needle biopsy subgroup.

Characteristics	Number of fragments									
	1	2	3	4	5	6	7	9	Overall	p
ME, n (%)	34 (58)	10 (17)	9 (15)	3 (5)	0	0	2 (3)	1 (2)	59 (100)	n.a.
AE, n (%)	18 (38)	21 (45)	4 (9)	2 (4)	1 (1)	1 (1)	0	0	47 (100)	
Preparation time (median)										
ME, s	55.5	55	77.5	84.5	n.a.	n.a.	111	70	73.5	0.511
AE, s	43.5	82	100	97	75	60	n.a.	n.a.	78.5	
Embedding time (median)										
ME, s	45	56	73	95	n.a.	n.a.	80.5	60	66.5 (+120)*	< 0.001
AE, s	5	5	5	5	5	5	n.a.	n.a.	5 (+40 [§])	
Trimming time (median)										
ME, s	34.5	32	17	28	n.a.	n.a.	31.5	22	29.7	0.016
AE, s	40	36	23.5	20	20	22	n.a.	n.a.	22.7	
Sectioning time (median)										
ME, s	23.5	28	47	41	n.a.	n.a.	46	28	34.5	0.897
AE, s	28	32	32.5	29.5	27	61	n.a.	n.a.	30.7	

*: supplement to adjust for cooling and scraping time of the cassette required for ME only; §: supplement if considering the whole AE procedure rather than the sole technician time; °: t-student test

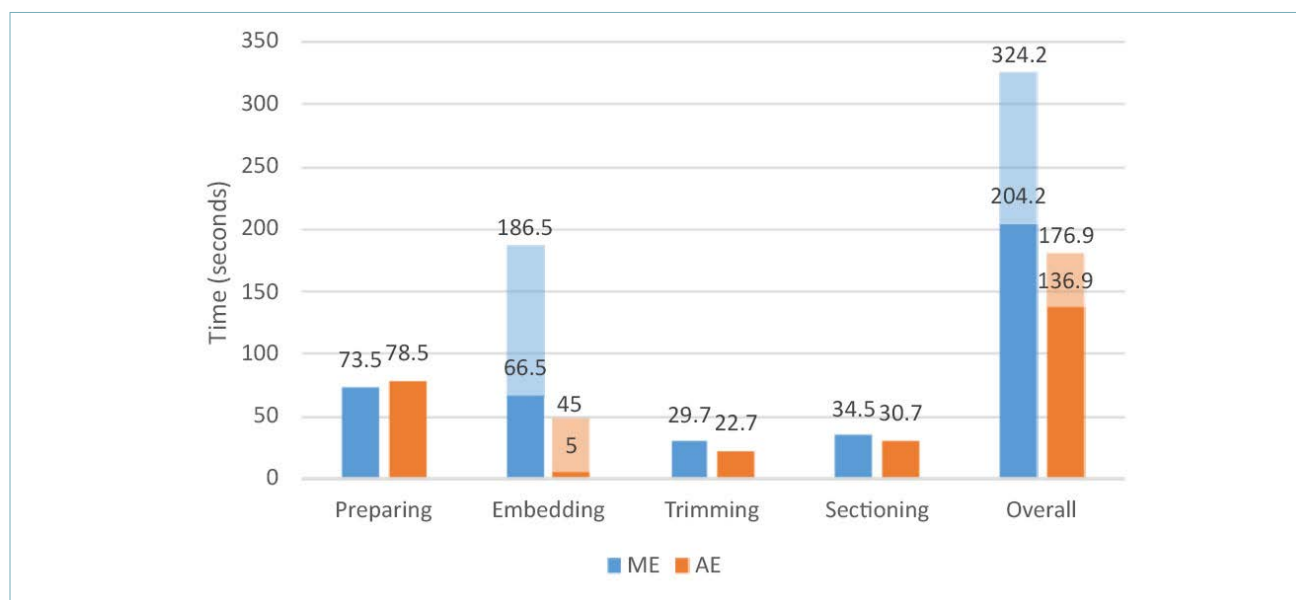


Figure 2. Graphic representation of the specific phases and overall timing for ME and AE for the needle biopsy subgroup. Solid histograms represent the time spent by technicians on the specific phase. Shaded histograms in the embedding phase and overall time represent the supplement time requested if considering cooling and scraping (+120 s) with the ME approach, and the procedure as a whole (+40 s) rather than the technician time with the AE approach.

ming, sectioning), thus resulting in an overall shorter time requirement for AE (150.2 s) compared to ME (250.4 s; Fig. 1).

NEEDLE BIOPSIES

We collected a total of 106 needle biopsies, further stratified into 59 ME and 47 AE cases. As with the endoscopic biopsy subgroup, times were recorded according to the number of fragments in each sample (Tab. III).

Overall, preparation time for needle biopsies increased with the number of fragments, although an inverse trend was observed in the highest fragment categories, likely affected by the small number of cases in these groups. Similar to endoscopic biopsies, embedding time was lower with AE (5+40 s compared with ME (66.5+120 s). Notably, for needle biopsy, trimming and sectioning were also faster with AE than ME (trimming: 22.7 s vs. 29.7 s; sectioning: 30.7 s vs. 34.5 s; Fig. 2).

TRANSURETHRAL SPECIMENS

A total of 62 TURB/TURP specimens were analyzed, further stratified into 12 ME and 50 AE cases. Analysis by number of fragments was not feasible, as all cases contained multiple fragments. Only overall median values were recorded (Tab. IV).

Preparation time per cassette was longer for ME

Table IV. Details of ME and AE timing for the TURB/TURP biopsy subgroup.

Preparation time	Median	p
ME, s	57.5	0.132
AE, s	47	
Embedding time		p
ME, s	105 (+120*)	< 0.001
AE, s	5 (+40 [§])	
Trimming time		p
ME, s	16	< 0.001
AE, s	27.5	
Sectioning time		p
ME, s	36.5	0.005
AE, s	30	

*: supplement to adjust for cooling and scraping time of the cassette required for ME only; §: supplement if considering the whole AE procedure rather than the sole technician time; °: t-student test.

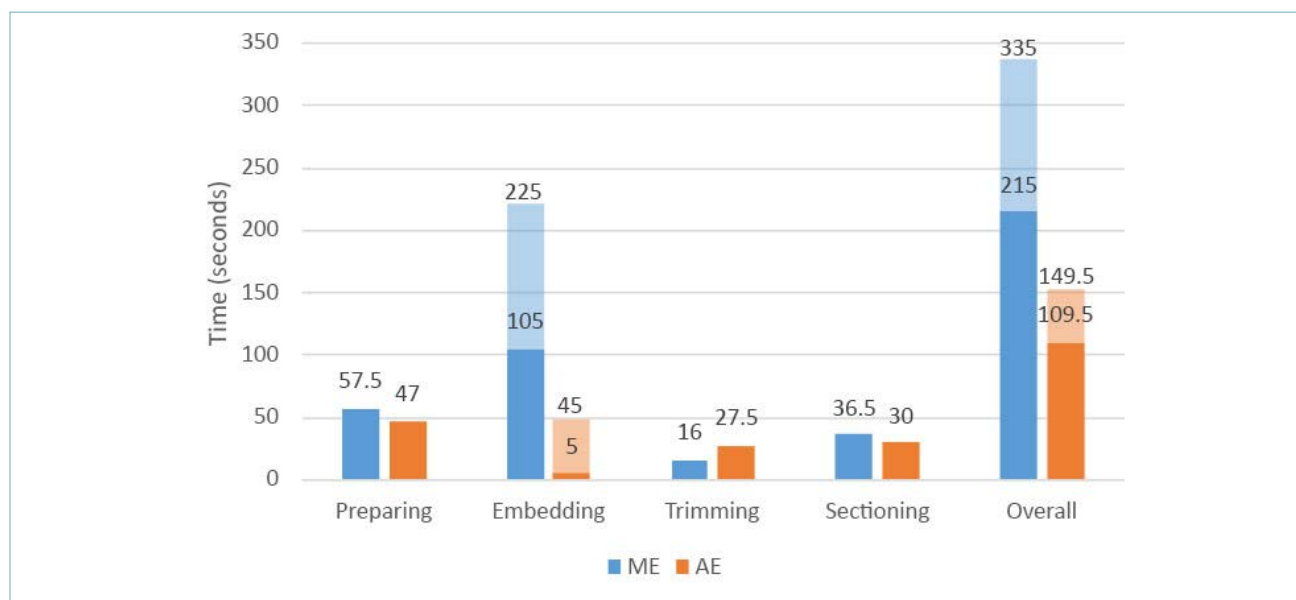


Figure 3. Graphic representation of the phases timing for ME and AE for the transurethral resection subgroup. Solid histograms represent the time spent by technicians on the specific phase. Shaded histograms in the embedding phase and overall time represent the supplement time requested if considering cooling and scraping (+120 s) with the ME approach, and the procedure as a whole (+40 s) rather than the technician time with the AE approach.

(57.5 s) than AE (47 s). AE substantially reduced embedding times (5+40 s) compared with ME (105+120 s), but trimming time was shorter for ME than AE (16s vs. 27.5 s). Overall, AE was significantly faster than ME ($p < 0.0001$; Fig. 3).

Discussion

This study demonstrated that AE significantly reduced technician procedural time compared to ME, both when considering the embedding phase alone and the entire workflow (preparation, embedding, trimming, and sectioning). These findings were consistent across all sample types analyzed (endoscopic biopsies, needle biopsies, and transurethral resections), but with specific caveats related to tissue and cassette characteristics.

For endoscopic biopsies, we noticed that the preparation time for one fragment (both for ME and AE) was higher than that for two or more fragments; cases with 5-6 fragments also showed increased preparation times. We looked for potential causes and observed that in cases with only one fragment, the biomedical technician lost time in checking whether a second fragment was present in the biopsy container. This is especially true, in our experience, for cervical biopsies (most of which are indeed one fragment per container), which are thin and semi-transparent, re-

quiring a double check. Trimming time also increased with the number of fragments for both methods, and, notably, AE trimming time (19.2 s) was longer than ME (12.7 s). In our opinion, this finding is related to the need to trim the cassette grid in AE. Similarly, sectioning times were slightly shorter for ME (39.5 s) compared to AE (41.5 s), as it was more difficult to obtain serial ribbon sections with AE. Sectioning times can also vary according to the specific protocol, including the number of slides, sections per slide, and section thickness, but these aspects were not considered in this study.

In needle biopsies, AE reduced embedding, trimming, and sectioning times. This evidence was most likely related to the fact that AE cassettes for needle biopsy have a finer mesh structure than those for endoscopy biopsy, which causes less resistance against the microtome blade. Moreover, the gel material provided with these cassettes determined a more precise positioning of the fragments, thus ensuring easier exposure during trimming. Published evidence demonstrated that AE-embedded biopsies reduced the need for re-embedding, further supporting our findings³.

For TURB/TURP specimens, AE reduced preparation time. However, since AE cassettes are less capacious, a larger number of them are required to process the same amount of tissue. This caveat deserves specific acknowledgment, as the total preparation time for AE cassettes may be longer when considering the overall

processing time per patient case rather than per cassette. AE also significantly reduced embedding time (5+40 s vs. 105+120 s for ME). Indeed, in our experience ME of this subgroup does not require particular precision but given the high number of fragments, care must be taken to avoid loss of tissue during sample handling. The trimming time for ME was shorter than that for AE, and, similar to endoscopic biopsies, we believe this difference can be explained by the coarser grid of AE cassettes that increases resistance during trimming. These sample timing differences between ME and AE for TURB/TURP samples were responsible for the unbalanced sample representation between the two subgroups. As mentioned in the method section, this study has been performed during routine daily activity of the pathology unit. Therefore, as samples were handled, we preferred prioritizing the diagnostic workflow rather than stalling sample handling to balance the subgroup representation. Beyond time savings, AE enabled reallocation of laboratory technicians. Whereas ME requires multiple technicians in the embedding phase, AE is largely independent, allowing staff to perform concurrent tasks and improving operational efficiency. In our unit, at least three laboratory technicians are simultaneously required for the embedding phases with the ME approach, as opposed to the AE approach, which re-

quires one technician only in the initial loading and final unloading phases. This aspect is particularly relevant in pathology units where staffing and workflow optimization are critical. Indeed, thanks to the implementation of AE in our tissue sample workflow, we redirected available technicians to the cutting phase (which was performed during the ME phase). This re-organization of the staff resulted in complete recover of “stalled” cases and achievement of an actual mean turnaround time of biopsy samples of two days (from grossing description to pathology report sign out) with no diagnostic delay.

Our single-centre study was limited by the exclusive focus on biopsies, which, however, represent the sample type where embedding is most crucial. In addition, while time savings were clearly demonstrated, a full cost-effectiveness analysis would require consideration of instrument purchase, maintenance, and consumables, which were outside the scope of this work. In particular, a dedicated cost analysis would be crucial: while forefront implementation of AE, as most innovative technologies, may be expensive, advantages become evident in the long-term (both in saved times, optimized workflow, and reallocated staff resources). We are currently collecting data and performing a cost-effect analysis of AE, as well as of the overall automated workflow of our unit, and we plan to present our data soon. From technical and educative perspectives, while the involvement of experienced technicians with dedicated training further reinforces the findings of our study (involvement of technician-in-training or students may have increased the time spent for ME and sample management), it would be interesting to compare AE and ME also with data of technicians in training. Finally, a more detailed analysis of tissue type (i.e., organ of origin) and related protocol (i.e., number of sections and stains) should give more in depth information on the use of AE. Comparison of tissue slide yield, from the pathologists' perspective, may also prove helpful (representative images of histochemical stains with AE and ME are reported in Figure 4).

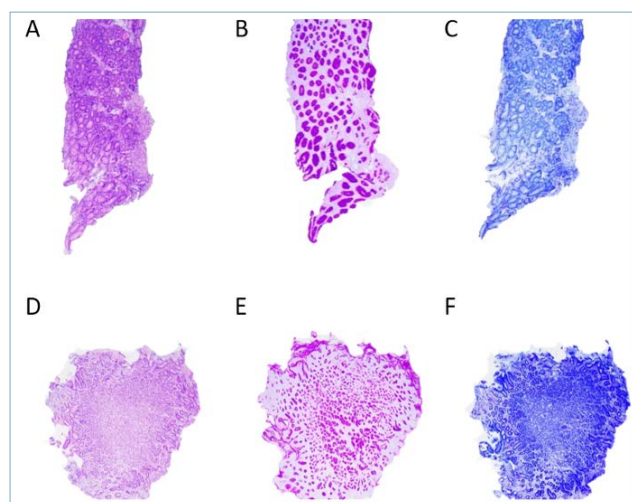


Figure 4. Representative images of histochemical stains following AE and ME (original magnification 40x, all images). A-C) Histochemical stains following AE, in particular hematoxylin and eosin (A), Alcian-BluPAS (B), and Giemsa (C). The blue arrow in each image indicate part of the Paraform used for AE. D-F) Histochemical stains following ME, in particular hematoxylin and eosin (D), Alcian-BluPAS (E), and Giemsa (F).

Conclusions

In conclusion, we demonstrated that AE significantly reduced embedding time compared to ME. In addition to the time gained alone, the advantage of reallocating technicians to other activities, instead of embedding, should also be stressed. To the best of our knowledge, this is the first report to quantitatively measure all tissue handling phases timing in a real-world daily routine diagnostic setting. Our results confirm the practical benefits of automation and provide evidence

to further support its broader adoption. Based on these data, our pathology unit is currently managing about 98% of samples with automated embedding. By demonstrating efficiency improvements, we advocate for increased automation of tissue sample embedding, enabling redeployment of laboratory technicians to other critical phases of the pathology unit workflow.

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CONFLICTS OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported.

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AUTHORS' CONTRIBUTIONS

Study conception and design: ZL, GF, ML; Data collection: ZL, BC, MP, TG, AV, PC, TM, BSA, MB, BS, GF and ML; Data analysis and interpretation: GA, ZL, and BC; Draft – Original writing: GA, GF, and ML. Draft – Review and Editing: GA, GF, and ML. All Authors reviewed and approved the final version of the manuscript.

ETHICAL CONSIDERATION

The study was conducted in accordance with the Declaration of Helsinki (1964) and its subsequent amendments. Written informed consent was waived, as the study involved no interventions impacting patient care.

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