All-Body-Cavity (ABC)-scopy: an approach for a feasible method of minimally invasive autopsy to allow for postmortem tissue sampling in cases where a conventional autopsy is denied

Lukas Rentschler, Bruno Märkl, Tina Schaller, Klaus Hirschbühl, Irene Kleinlein, Sebastian Dintner, Johanna Waidhauser, Sebastian Wolf, Christian Golling, Dmytro Vlasenko

Angaben zur Veröffentlichung / Publication details:

Rentschler, Lukas, Bruno Märkl, Tina Schaller, Klaus Hirschbühl, Irene Kleinlein, Sebastian Dintner, Johanna Waidhauser, Sebastian Wolf, Christian Golling, and Dmytro Vlasenko. 2023. "All-Body-Cavity (ABC)-scopy: an approach for a feasible method of minimally invasive autopsy to allow for postmortem tissue sampling in cases where a conventional autopsy is denied." *Pathology - Research and Practice* 241: 154263. https://doi.org/10.1016/j.prp.2022.154263.

Pathology - Research and Practice 241 (2023) 154263

Contents lists available at ScienceDirect

Pathology - Research and Practice

journal homepage: www.elsevier.com/locate/prp

All-Body-Cavity (ABC)-scopy—An approach for a feasible method of minimally invasive autopsy to allow for postmortem tissue sampling in cases where a conventional autopsy is denied

Lukas Rentschler [a,*], Bruno Märkl [a], Tina Schaller [a], Klaus Hirschbühl [b], Irene Kleinlein [a], Sebastian Dintner [a], Johanna Waidhauser [b], Sebastian Wolf [c], Christian Golling [c], Dmytro Vlasenko [c]

[a] Pathology, Medical Faculty, University of Augsburg, Augsburg, Germany
[b] Hematology and Oncology, Medical Faculty, University of Augsburg, Augsburg, Germany
[c] General, Visceral and Transplantation Surgery, University Hospital of Augsburg, Augsburg, Germany

ARTICLE INFO

Keywords:
Autopsy
Minimal invasive
Laparoscopy

ABSTRACT

Objectives: The decreasing autopsy numbers in many western countries have been partially attributed to the invasiveness of the autopsy, which causes relatives to decline postmortem examination. This issue has been addressed by developing methods of minimally or non-invasive autopsy, which could be shown to increase acceptance for autopsies. The aim of this study is to compare the All-Body-Cavity-scopy (ABC-scopy) to conventional autopsies for diagnostic accuracy.

Methods: The ABC-scopy is an endoscopic approach for minimally invasive autopsy involving laparoscopic and thoracoscopic evaluation of the accessible organs, followed by excision biopsies of relevant organs and conspicuous findings. The method was performed in 10 cases on deceased patients scheduled for autopsy, each followed by a conventional autopsy.

Results: The results gathered from ABC-scopy through observation and histopathological evaluation provided an acceptable diagnostic accuracy in 9 out of 10 autopsies when compared to those of the conventional autopsy for diagnostic findings.

Conclusions: The ABC-scopy is a feasible approach for minimally invasive autopsy that provides acceptable diagnostic value. Despite its minimally invasive nature, the procedure enables representative histology through providing large size excision biopsies from intraabdominal and thoracic organs, which is especially useful for examining disseminated diseases such as metastasized tumors.

1. Introduction

Autopsies play an important role in the critical evaluation of premortem diagnoses and therapeutic decisions. Despite modern imaging and instrumental diagnostics, significant discrepancies between clinical and autopsy diagnoses can still be found frequently [1].

Tissue samples gathered during autopsies can also prove essential for better understanding of new or rare diseases. This has become especially apparent during the ongoing COVID-19 pandemic [2–7]. They can also be useful to determine extent and heterogeneity in metastasized tumor patients.

In Germany, as in many other countries, clinical autopsies are usually performed at the request of the most recently treating physicians, as long as the relatives of the deceased have no reservations. In times of generally decreasing autopsy numbers [8,9], one way to improve autopsy rates was shown to be through better coordination with clinicians [10]. However, autopsies are still frequently denied by relatives of the deceased who have major reservations about postmortem necropsy.

To address this issue, it has recently been shown that the availability of a minimally invasive autopsy (MIA) technique can significantly increase autopsy numbers overall, particularly among people with a non-Western European ethnic background [11,12].

Different methods of non- or minimally invasive autopsy have been

* Correspondence to: Department of Pathology and molecular Diagnostics, University Hospital Augsburg, Stenglinstr. 2, 86156 Augsburg, Germany.
E-mail address: Lukas.rentschler@uk-augsburg.de (L. Rentschler).

https://doi.org/10.1016/j.prp.2022.154263
Received 27 October 2022; Received in revised form 2 December 2022; Accepted 3 December 2022
Available online 6 December 2022

described. In recent decades the focus has been predominantly on postmortem cross sectional imaging using CT and/or MRI, with or without obtaining needle biopsies [13]. Individual studies on ultrasound-based methods have also been conducted [14,15].

To date, and to the best of our knowledge, only a very limited number of studies have been conducted that explore the feasibility of performing autopsies by using endoscopy and instruments of minimally invasive surgery [13]. Those studies that have been conducted had their focus largely on macroscopic findings, sometimes including smaller biopsies [16–19].

The aim of this study was to establish an endoscopy-based autopsy method that allows for post-mortem tissue sampling and macroscopic evaluation, for cases where the relatives of the deceased limit the autopsy to a MIA. In order to test the new method for its diagnostic value, the ABC-scopy was tested for diagnostic reliability against the gold standard of a conventional autopsy in 10 cases in which the relatives allowed for both procedures to be performed. An emphasis was put on obtaining sizeable biopsies, enabling diagnostically conclusive histology.

2. Material and methods

2.1. Collection

This study was conducted at the Department of Pathology and Molecular Diagnostics of the University Hospital Augsburg. Included were only deceased patients of the University Hospital Augsburg, for whom a regular clinical autopsy was requested, and after the relatives agreed to participation in the study. There was no selection made among the patients, other than availability of staff and timing so that the conventional autopsy was not delayed for more than one day.

This study was conducted in accordance with the Declaration of Helsinki and under ethics approval granted by the Ethics Committee of the Faculty of Medicine, Ludwig-Maximilian-University, Munich (No. 21–0527).

2.2. Autopsy - technique and sample processing

Endoscopic autopsies were performed by a pathology resident and a board-certified visceral surgeon. The pathology resident performed 4 h of training on a laparoscopy trainer prior to the first autopsy. Conventional autopsies were performed by two pathology residents with one or two assistant prosectors with support by a board-certified pathologist.

Prior to the beginning of the autopsy, the clinical diagnoses and questions for the autopsy were studied as well as radiological imaging if available.

For endoscopic visualization, a laparoscopy stack consisting of a carbon dioxide insufflator, cold light source, camera, and monitor was used. The video signal from the camera was recorded throughout the autopsy for documentation purposes.

Recovered tissue samples were fixed for at least 48 h in a 4% formaldehyde solution.

Pleural or abdominal effusions were sampled for cytologic evaluation in cases where there was suspicion of malignant effusions. The samples were stored refrigerated (approximately 12 h) until processing for regular cytologic smears that were stained with Giemsa.

The ABC-scopy was usually performed in the evening of the day that the autopsy was requested on, and documented for the macroscopic findings afterwards. On the next day, a conventional full autopsy was performed and documented separately. Tissue samples of the same organs sampled during the ABC-scopy were collected for comparison.

To ensure no critical information was lost, one physician was present during both procedures and the resected tissue was made available for evaluation.

Histologic sections were stained in H&E, as well as Elastica-Van Gieson, Berlin blue, and Periodic acid-Schiff for certain tissues. The histologic slides obtained from both endoscopic and conventional autopsy were evaluated by senior pathologists. Immunohistochemistry and molecular diagnostics were performed when necessary.

In order to test the quality of the samples for potential molecular analysis, RNA and DNA were extracted from FFPE-material. Using the *Maxwell RSC RNA FFPE*-Kit and the *Maxwell FFPE Plus DNA*-Kit respectively, nucleic acids were extracted from liver and lung tissue that was gathered during the ABC-scopy and during the conventional autopsy. RNA and DNA samples were then tested on a *2100 Agilent Bioanalyzer, Agilent, Santa Clara, CA, USA* for integrity using the *DNA 7500 Kit* and the *RNA 6000 Nano Kit* respectively according to the instructions provided in the manual.

2.3. Grading of diagnostic reliability

For evaluating the diagnostic reliability of the endoscopic technique, the diagnoses from the ABC-scopy were compared to those found in the conventional autopsy. The reliability was only evaluated for diagnoses found in thoracic and intraabdominal organs which are accessible with the ABC-scopy. The individual autopsies were grouped in three grades by conformity of main findings (i.e., cause of death or extensive tumorous diseases) as well as relevant comorbidities and incidental findings. Grade 1 represented a complete conformity between the endoscopic findings and the subsequent conventional autopsy, including all relevant diagnoses and incidental findings. Grade 2 was attributed to cases where the most important diagnoses, especially those considered as cause of death were found, but relevant comorbidities (e.g. pulmonary metastases or incidental prostate cancer) remained undetected. Grade 3 was attributed where only some incidental findings could be found but the most important diagnoses were not detected.

3. Results

3.1. Establishing the method

After an initial external inspection of the corpse and confirmation of death, the patient's body was placed on the autopsy table in supine position. The laparoscopy stack was located to the right of the patient's body. To examine the intra-abdominal and retroperitoneal organs, three basic accesses were initially created via 12 or 15 mm trocars. The first trocar was inserted periumbilically through a small incision, and used to establish a capnoperitoneum up to a pressure of 20 mmHg and introduce the camera. Two additional 12 mm working trocars were placed in the right and left mid-abdomen in the projection of the medioclavicular line, providing access to the entire abdomen. In the case of anatomical difficulties (i.e., visceral adiposity or adhesions), one more 5-mm trocar was inserted. After placement of the trocars, the autopsy was started with inspection of the abdomen, including photo- and video-documentation of the visible organs as well as documentation of abdominal effusion. (Fig. 1).

Subsequently, targeted organ biopsies for histological diagnostics were obtained. For access to the spleen and retroperitoneal organs such as left kidney, left adrenal gland, or pancreatic tail, the patient's corpse was moved into a right lateral position. One additional 5 mm trocar was placed in the projection of the anterior axillary line to provide better access for tissue sampling.

For paired organs such as the kidneys, adrenal glands, or lungs, usually only one side was examined and exemplarily biopsied in order to save time and effort. The left kidney and adrenal gland were always preferred for easier accessibility. Both sides were examined in cases where there was suspicion of unequal findings based on premortem diagnoses or imaging. (Fig. 2, A-C).

The examination of the thoracic and mediastinal organs was performed in the same way as the abdominal autopsy. The patient's body stayed in right lateral position. Three 12 or 15 mm trocars were placed, one each in the 6th intercostal space (ICS) on the projection of the medio

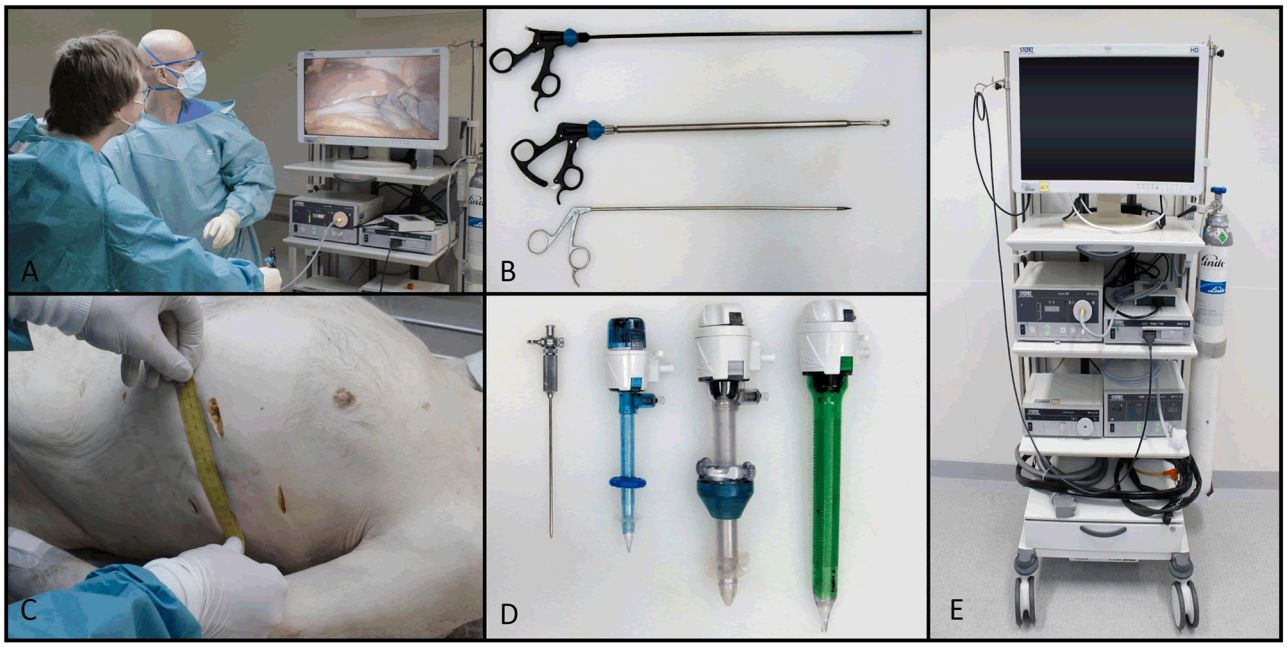


Fig. 1. Setting and material used during ABC-scopy, A: setting for ABC-scopy, inspection of upper abdominal organs with laparoscopy stack, on the monitor liver with metastases; B: instruments used during ABC-scopy; C: Thoracic skin incisions for ABC-scopy, note the largest incision (ca. 3.5–4 cm) used for biopsy retrieval; D: trocars used for ABC-scopy; E: laparoscopy stack with monitor.

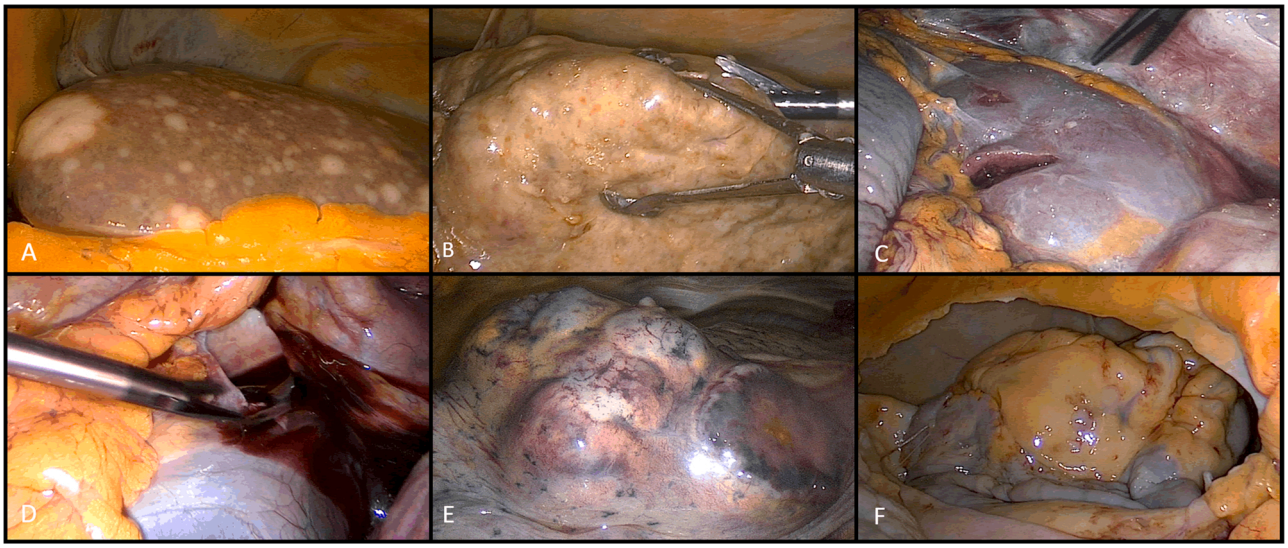


Fig. 2. Exemplary endoscopic views, A: liver with multiple metastases; B: taking of an excision biopsy of a liver with cirrhosis; C: view on the left kidney; D: draining of a hemopericardium; E: lung with voluminous metastases; F: view through pericardial opening on right heart with epicardial tumor nodes.

clavicular line and the 5th and 8th ICS of the medial axillary line or nearby positions depending on accessibility.

After macroscopic evaluation of the left lung and pleura as well as documentation of pleural effusion, the pericardium was opened by incision. Presence or absence of pericardial effusion was documented. Subsequently an exemplary biopsy of the ventricular wall was taken, allowing for histologic evaluation of myocardial changes associated with hypertrophy or cardiomyopathies. In some cases, it was also possible to get a macroscopic and subsequently histologic impression of the presence and grade of coronary sclerosis. Finally, the left lung and any macroscopically conspicuous findings were biopsied. In most cases, the opening of the right chest was spared. Both in cases where it was impossible to examine the left chest properly due to adhesions and in cases where there was pre-mortem suspicion of meaningful additional findings in the right pleural cavity, the patient's body was moved into a left lateral position and the same procedure as described for the left side was performed. (Fig. 2, D-F).

3.2. Sample generation

Biopsies were usually taken as excision biopsies and recovered directly with a forceps through the skin incision, sparing an extraction bag. Alternatively, small forceps biopsies could be obtained for lesions that were too difficult to reach. The decision on the size, number, and exact location of tissue samples taken was made depending on the premortal clinical diagnoses and questions, in addition to available radiological imaging and macroscopic findings during the ABC-scopy. Biopsies were routinely taken of liver, spleen, pancreas, kidney,

adrenal gland (when possible), lung, and heart. Samples were usually generated as excision biopsies of a size up to 5 × 2.5 × 2.5 cm for solid parenchymatous organs (e.g. liver or kidney) and up to 9 × 6×3 cm for softer tissue (especially pulmonary tissue), allowing for large histologic sections of high quality. The limiting factor for the size of biopsies was the diameter of the largest skin incision. (Fig. 3).

3.3. Feasibility and learning curve

A total of 10 autopsies were performed, with a median duration of 123 min (range 100–155 min). Laparoscopy and at least unilateral thoracoscopy were performed in every case. Bilateral thoracoscopy was performed in 3 cases.

Over the course of 10 autopsies, the pathology resident was able to take over more tasks. In the end, the thoracic and upper abdominal organs were evaluated and biopsied solely by the resident, while the retroperitoneal organs such as pancreas, kidney, or adrenal gland sometimes still required assistance. In cases with highly obese patients, laparoscopy in particular proved much more difficult.

In patients that had undergone previous surgery, adhesions could limit visibility and accessibility. In one case of a patient with a history of unilateral pleurodesis, no adequate sample generation on that side was possible.

3.4. Reliability

When grading the ten individual autopsies by diagnostic reliability, six of them could be grouped into grade 2, three cases were grouped into grade 1, and one autopsy was considered grade 3. (Table 1).

In addition, the autopsy findings of both procedures were grouped by diagnoses and compared between the ABC-scopy and the conventional autopsy. A high reliability of 100% could be shown for diagnoses such as myocardial hypertrophy, when assessed by histological criteria or diffuse fibrosis as well as for pneumonia or tumor infiltration of the liver. Other diagnostic findings like pulmonary or peritoneal metastases were only found in a limited number of cases in the ABC-scopy, while some findings like prostate cancer or renal papillary adenomas were exclusively detected in conventional autopsy. (Table 2).

3.5. Sample quality

The extracted nucleic acids from FFPE lung and liver tissue showed a relatively high degree of fragmentation for samples from both autopsy techniques when tested on the *2100 Agilent Bioanalyzer*. The RNA fragment lengths were shown to be largely under 500 nucleotides, (Graph 1) with RIN (RNA integrity number) values of 1.5–2.4, which shows a high degree of degradation [20]. There was no relevant difference between the samples from the different autopsy techniques.

4. Discussion

In this study we present a technique using endoscopy and instruments of minimal invasive surgery to perform minimal invasive autopsies, which is especially useful in cases where postmortem tissue sampling is needed for scientific purposes. It is not thought to serve as a competitive alternative to conventional autopsy but as a chance to obtain tissue samples and limited diagnostic findings, in cases where the next of kins deny a conventional autopsy.

4.1. Comparison to other minimally invasive approaches

In this study, we were able to show that the ABC-scopy can produce reliable diagnostic findings in patients with abdominal or thoracic pathologies. Specifically, the large size of the excision biopsies proved crucial for high quality in diagnostic histology. Thus, it allows for acceptable reliability, especially for disseminated diseases such as pneumonia, extensively metastasized tumor diseases, or myocardial hypertrophy and fibrosis. Adequacy of the tissue for diagnostic histologic examination was given in all cases. Although the relatively small number of cases included in this study brings limitations to generalize the findings, the method of direct vision control via the endoscope during the sample generation makes inadequate tissue quantity or quality unlikely. In contrast, MIA techniques using needle biopsies, especially when performed blindly (without imaging technique, e.g. CT), are more likely to produce some amount of inadequate samples [21]. This could be due to missing lesions or due to sampling non representative tissue (e.g., necrosis).

In a systematic review of non- or minimally invasive autopsy

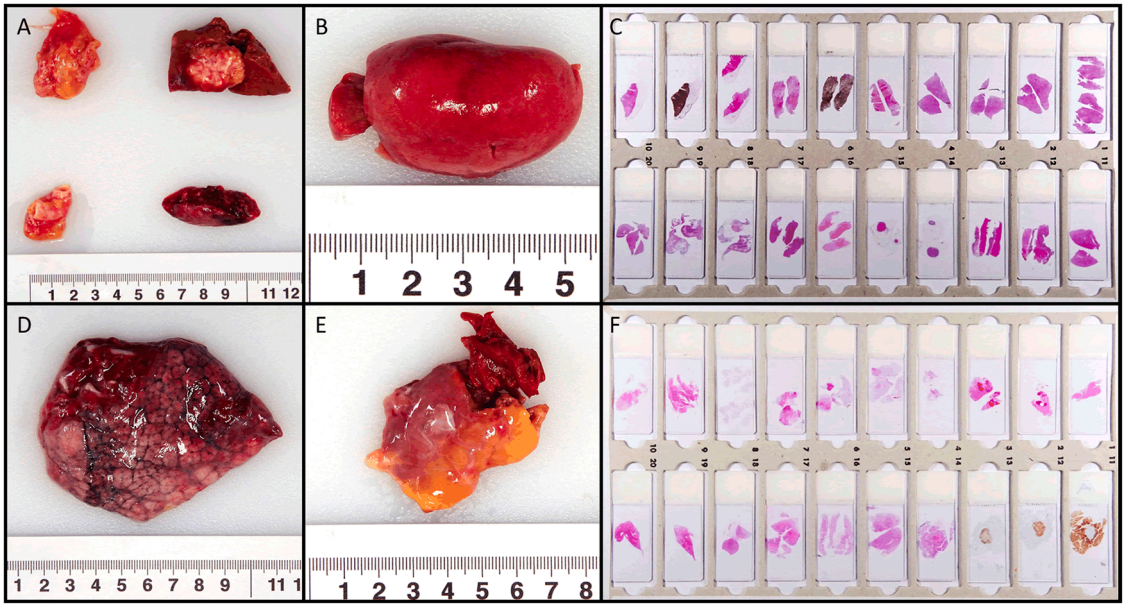


Fig. 3. Exemplary excision biopsies taken during ABC-scopy (sizes for scale in cm), A: From top, left to right: pancreas, liver biopsy with metastasis, splenic artery with calcifications, splenic tissue; B: left Kidney; D: lung tissue (upper left lobe); E: myocardial tissue; C and F: exemplary histologic sections stained in H&E, Elastica Van Gieson and immunostains.

Table 1
Comparing premortal clinical diagnoses with major diagnoses found in ABC-scopy, and relevant deviations between ABC-scopy and conventional autopsy findings for each autopsy performed. Abbreviations: CUP: cancer of unknown primary, AML: acute myeloid leukemia, DIP/RB-ILD: desquamative interstitial pneumonia here possibly related to respiratory bronchiolitis interstitial lung disease.

#	Age (in decades)	Sex	Relevant clinical diagnoses	Major diagnoses found or confirmed in ABC-scopy	Relevant deviations in abdominal or thoracic cavity between ABC-scopy and conventional autopsy	Final cause of death	Grade of deviation
1	7th	M	rectal carcinoma, diabetes, hypertension	hepatic and peritoneal metastasized colorectal cancer, multiple older myocardial infarctions, calcified arteriosclerosis	solitary pulmonary metastasis was not detected, primary tumor was not examined	cardiac failure due to multiple older myocardial infarctions and progressed tumor disease	Grade 2
2	6th	M	liver cirrhosis with hepatorenal syndrome	liver cirrhosis, gastric ulcer, intrahepatic cholangiocarcinoma with pulmonary metastases	no relevant deviations found in abdominal or thoracic organs	liver cirrhosis with hepatorenal syndrome	Grade 1
3	6th	M	pulmonary metastasized salivary gland carcinoma	pulmonary and hepatic metastasized CUP* with known manifestation of the parotid gland and extensive cancer manifestation of the pancreas	no relevant deviations found in abdominal or thoracic organs	respiratory failure due to extensively pulmonary metastasized cancer	Grade 1
4	5th	F	AML* * with leptomeningeal manifestation, pneumonia	DIP/RB-ILD* ** , arteriosclerosis	no relevant deviations found in abdominal or thoracic organs	tonsillar herniation following intrathecal therapy of AML	Grade 2
5	5th	M	peritonitis with intestinal pneumatosis, chronic pancreatitis	acute peritonitis with massive bacterial growth, hepatomegaly, chronic pancreatitis	gastric ulcer with vascular erosion was not detected	fulminant sepsis due to acute peritonitis (reason for peritonitis remained unclear)	Grade 2
6	7th	M	metastasized neuroendocrine carcinoma of the lung, bicytopenia	hepatic, pancreatic and pulmonary metastasized small cell cancer (lung) with pericardial infiltration	hilar lymph node metastases were not detected	cardiopulmonary failure due to progressed tumor disease	Grade 2
7	5th	F	acute cardiac death, differential diagnoses: pulmonary embolism vs. aortic dissection	cardiac tamponade with hemopericardium, myocardial hypertrophy, fatty liver disease	aortic dissection was not proven directly, gastric leiomyoma was not detected	cardiac tamponade due to aortic dissection	Grade 2
8	6th	M	sinus vein thrombosis, cerebral infarction, metastasized prostate cancer	older peripheral pulmonary embolisms, myocardial hypertrophy	residual prostate cancer was not detected	intracerebral hemorrhage due to leptomeningeal cancer with sinus vein thrombosis	Grade 3
9	7th	M	sepsis with bacteremia, unclear infectious focus, paralytic ileus	acute bronchopneumonia, fatty liver disease, distension of small intestine	erosive esophagitis and incidental prostate cancer were not detected	sepsis with pneumonia	Grade 2
10	7th	M	aspiration, coronary heart disease, congestive heart failure, atrial fibrillation	incarcerated inguinal hernia, acute pneumonia	aspiration was not proven, sizeable (5 mm) myocardial scar was not detected	hypoxia and aspiration pneumonia related to incarcerated inguinal hernia	Grade 2

*CUP: cancer of unknown primary, * *AML: acute myeloid leukemia, * **DIP/RB-ILD: desquamative interstitial pneumonia here possibly related to respiratory bronchiolitis interstitial lung disease

techniques, Blokker et al. describe that minimally invasive techniques surpass non-invasive (imaging only) approaches in diagnostic accuracy [13], thus supporting the importance of histologic examination. They also find that image guided biopsies are superior to blind needle biopsies and that cross-sectioning imaging (CT or MRI) is superior to ultrasound imaging. In addition, MIA using MRI, CT and CT-guided biopsies could be shown to even produce a higher yield of postmortem diagnoses than conventional autopsies [22]. In a clinical setting, these cross-sectioning technologies have the limitation that the machines required are expensive and primarily used for the living patients; therefore they only have limited availability for examining the deceased. In our setting, the laparoscopy tower was permanently available at the department of pathology and exclusively used for ABC-scopy.

When it comes to quality of autopsy tissue samples for molecular analyses, the high degree of degradation, especially of RNA samples, can limit the diagnostic value in certain applications. However, in our experience, autopsy material can still be suitable for many applications, such as immunohistochemistry, RNA-in-situ-hybridization [6], RT-PCR [23] or even Next Generation Sequencing [24].

There is no good reason why the specific technique of tissue sampling should have an influence on quality of RNA or DNA. However, the time between death and autopsy could have a meaningful impact. In addition, tissue processing and storage other than FFPE, such as direct freezing [25] or sample preservation in phenol-chloroform solutions (e.g. TRIzol) could potentially produce less degraded nucleic acids.

4.2. Limitations

To prevent loss of information due to the large biopsies taken, the pathology resident performing the conventional autopsy was not blinded to the results of the ABC-scopy which poses a threat to unbiased results.

While the ABC-scopy provides an acceptable reliability on confirming and determining (postmortem) diagnoses, it has a clear limitation in excluding some common causes of death. Although diagnoses such as pulmonary embolisms or myocardial infarctions could be detected in excision biopsies, the absence of those cannot be confirmed with enough certainty. Specifically, the examination of the heart and associated vessels is strongly limited compared to conventional autopsies, with myocardial lesions usually not macroscopically visible during the endoscopy. In this case the ABC-scopy relies largely on coincidental findings in exemplary biopsies. The lack of information about organ weights also made it necessary to refer to microscopic changes to assess myocardial hypertrophy such as myocyte hypertrophy.

In addition, any cerebral lesions will remain entirely undetected due to the technical limitation to intraabdominally and intrathoracically located organs. Intracranial causes of death, which are a frequent differential diagnosis for unknown causes of death, can therefore not be excluded with a MIA restricted to ABC-scopy.

The availability of the equipment and the training effort for the staff are certainly a considerable limitation for the implementation of the technique at other hospitals and will likely require a well working

Table 2
Comparison of how frequently each specific diagnosis was detected in autopsies using ABC-Scopy and conventional autopsy.

Findings	ABC-scopy	Conventional autopsy	Ratio
myocardial hypertrophy	8	8	8/8
myocardial scarring/fibrosis	5	5	5/5
pneumonia	3	3	3/3
liver metastases/ tumor	3	3	3/3
fatty liver disease	3	3	3/3
interstitial nephritis	3	3	3/3
pleural metastases	2	2	2/2
pericardial metastases	1	1	1/1
pancreatic tumor	1	1	1/1
pancreatitis	1	1	1/1
peritonitis	1	1	1/1
liver cirrhosis	1	1	1/1
inguinal hernia	1	1	1/1
hemopericardium	1	1	1/1
pulmonary metastases	3	4	3/4
peritoneal metastases	1	2	1/2
splenic infarction	1	2	1/2
lymph node metastases	1	1	*
gastric ulcer	1	1	*
gastric leiomyoma	0	1	0/1
intestinal adenomas	0	1	0/1
rectal cancer	0	1	0/1
aspiration	0	1	0/1
esophagitis	0	1	0/1
aortic dissection	0	1	0/1
prostate cancer	0	2	0/2
renal papillary adenoma	0	2	0/2

*a gastric ulcer as well as lymph node metastases were each found in one case during ABC-scopy and fully resected, thus not available for finding during the full autopsy anymore. Therefore, an accurate ratio cannot be determined.

cooperation between the pathologic and surgical departments.

4.3. Outlook

For future applications of the ABC-scopy as a MIA, a combination with postmortem cross-sectioning imaging such as CT could improve the diagnostic abilities vastly. By enabling the detection of intracranial lesions, potentially combined with tissues sampling through a small drill hole, intracranial causes of death could be confirmed or excluded.

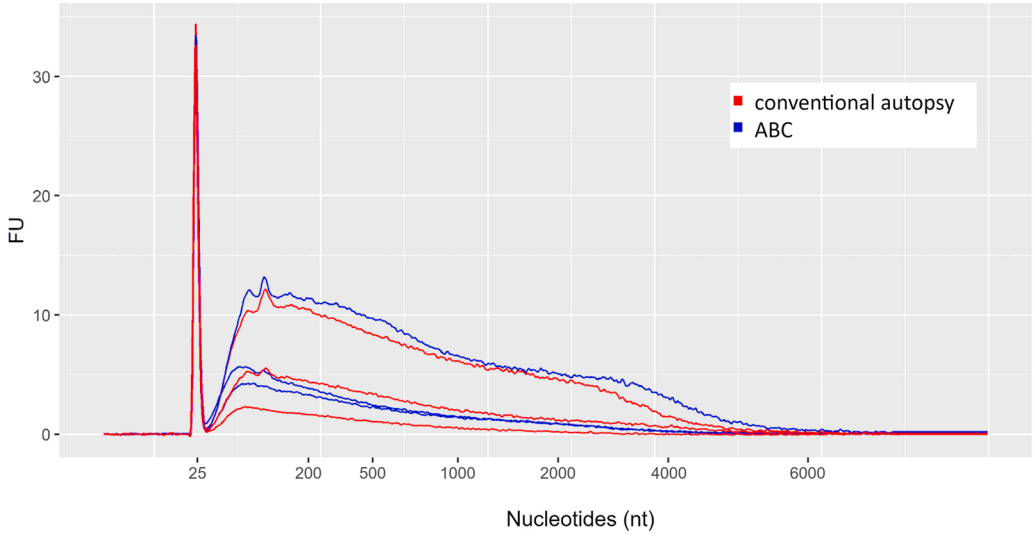
The unilateral exploration of paired organs, as performed here, precludes incidental clinically unsuspected findings on the side that was not sampled. In order to not miss incidental lesions due to unilateral sampling, a complete bilateral sampling of paired organs could be considered for future applications. For gaining access to and sampling of the right kidney and adrenal gland, an approximate 20–30 min of additional time for the ABC-scopy as well as one additional trocar should be calculated. The bilateral thoracic exploration was performed 3 times within this study and lengthened the procedure by approximately 20 min. Cross sectioning imaging, whether it be performed post mortal or even premortal, could be another possible way to decide whether the additional effort is justified or not.

5. Conclusion

While the conventional autopsy is the gold standard, ABC-scopy is a feasible approach for minimally invasive postmortem examination in cases where the relatives of the deceased limit the autopsy to a MIA, despite a careful explanation of the conventional technique. In such cases, it offers a valuable visually conducted approach to obtain liquids and large tissue samples. It should not be preferred over a conventional autopsy when there are no limitations to the method of autopsy. Other than primary clinical interest for postmortem examination, possible applications for the ABC-scopy could be cases where there is a scientific interest in gaining visual proof and tissue samples from deceased when the autopsy is limited to a MIA. This can apply for tumor studies as well as in the case of rare or new diseases, such as during the first waves of the COVID-19 pandemic, when knowledge about the actual effects that the virus had on the body were demanded quickly. However, it should be noted that some important findings, such as the extent of the increase in deep venous thrombosis and venous thromboembolisms [26] would not have been detected with ABC-scopy alone.

CRediT authorship contribution statement

L. Rentschler: Writing – original draft, Methodology, Investigation, **D. Vlasenko:** Methodology, Investigation, **B. Märkl:** Writing – review & editing, Conceptualization, Supervision, **T. Schaller:** Conceptualization, **K. Hirschbühl:** Conceptualization, **I. Kleinlein:** Data curation, Investigation. **S. Dintner:** Data curation, **J Waidhauser:** Resources, **S. Wolf:** Investigation. **C. Golling:** Resources; All authors were involved in writing the paper and had final approval of the submitted and published versions.



Graph 1. Fragment lengths for RNA samples from lung tissue collected during ABC-scopy and conventional autopsy. The x-axis shows fragment lengths in nucleotides, the y-axis fluorescence units (FU).

Declaration of Competing Interest

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

Acknowledgments

The authors are thankful to Silvia Miller, Francisco Farfán-Lopez and Andrea Maccagno for conducting the conventional autopsies, Dr. Theodor Wagner and Dr. Bei Huang for supervising autopsies, Kai Hebick, Annalena Schmidt and Max Bader for assisting in conventional autopsies and Andrea Seuser for excellent technical assistance. The authors are particularly grateful to all relatives who gave their consent for the autopsies.

Disclosure

All the authors declare that they have no conflicts of interest. No external funding was received.

Declarations of interest

none, no external funding was received.

References

[1] F. Tavora, C.D. Crowder, C.C. Sun, A.P. Burke, Discrepancies between clinical and autopsy diagnoses: a comparison of university, community, and private autopsy practices, Am. J. Clin. Pathol. 129 (1) (2008), 102-9.
[2] A.N. Duarte-Neto, R.A.A. Monteiro, L.F.F. da Silva, D. Malheiros, E.P. de Oliveira, J. Theodoro-Filho, et al., Pulmonary and systemic involvement in COVID-19 patients assessed with ultrasound-guided minimally invasive autopsy, Histopathology 77 (2) (2020), 186-97.
[3] P. Boor, P. Eichhorn, A. Hartmann, S.F. Lax, B. Markl, T. Menter, et al., Practical aspects of COVID-19 autopsies, Pathologe 42 (2) (2021) 197–207.
[4] K. Hirschbuhl, S. Dintner, M. Beer, C. Wylezich, J. Schlegel, C. Delbridge, et al., Viral mapping in COVID-19 deceased in the Augsburg autopsy series of the first wave: A multiorgan and multimethodological approach, PLoS One 16 (7) (2021), e0254872.
[5] K. Hirschbuhl, T. Schaller, B. Markl, R. Claus, E. Sipos, L. Rentschler, et al., High viral loads: what drives fatal cases of COVID-19 in vaccinees? - an autopsy study, Mod. Pathol. (2022).
[6] T. Schaller, B. Markl, R. Claus, L. Sholl, J.L. Hornick, M.P. Giannetti, et al., Mast cells in lung damage of COVID-19 autopsies: a descriptive study, Allergy (2022).
[7] D. Jonigk, C. Werlein, T. Acker, M. Aepfelbacher, K.U. Amann, G. Baretton, et al., Organ manifestations of COVID-19: what have we learned so far (not only) from autopsies? Virchows Arch. (2022).
[8] M. Grassow-Narlik, M. Wessolly, J. Friemann, Autopsy rates in Germany, Pathologe 38 (5) (2017), 422-9.
[9] F. Erlmeier, W. Weichert, R. Knüchel, J. Andruszkow, Erwachsenenobduktionen im letzten Jahrzehnt in Deutschland, Der Pathol. 38 (5) (2017), 430-7.
[10] J. Waidhauser, B. Martin, M. Trepel, B. Markl, Can low autopsy rates be increased? Yes, we can! Should postmortem examinations in oncology be performed? Yes, we should! A postmortem analysis of oncological cases, Virchows Arch. (2020).
[11] I.M. Wagensveld, A.C. Weustink, J.A. Kors, B.M. Blokker, M.G.M. Hunink, J. W. Oosterhuis, Effect of minimally invasive autopsy and ethnic background on acceptance of clinical postmortem investigation in adults, PLoS One 15 (5) (2020), e0232944.
[12] I.M. Wagensveld, M.G.M. Hunink, P.A. Wielopolski, F.J. van Kemenade, G. P. Krestin, B.M. Blokker, et al., Hospital implementation of minimally invasive autopsy: A prospective cohort study of clinical performance and costs, PLoS One 14 (7) (2019) e0219291.
[13] B.M. Blokker, I.M. Wagensveld, A.C. Weustink, J.W. Oosterhuis, M.G. Hunink, Non-invasive or minimally invasive autopsy compared to conventional autopsy of suspected natural deaths in adults: a systematic review, Eur. Radiol. 26 (4) (2016), 1159-79.
[14] O.R. Brook, K.G. Piper, N.B. Mercado, M.S. Gebre, D.H. Barouch, K. Busman-Sahay, et al., Feasibility and safety of ultrasound-guided minimally invasive autopsy in COVID-19 patients, Abdom. Radiol. 46 (3) (2021), 1263-71.
[15] P. Boor, P. Eichhorn, A. Hartmann, S.F. Lax, B. Markl, T. Menter, et al., Praktische Aspekte von COVID-19-Obduktionen, Pathologe 42 (2) (2021) 197–207.
[16] R.W.S. Avrahami, E. Daniels-Philips, T. Kahana, J. Hiss, Endoscopic autopsy, Am. J. Forensic Med. Pathol. 16 (1995), 147–50.
[17] Ram Avrahami M.S.W., M.D.; Yuda Hiss, M.D.; Alexander A. Deutsch, MD, FRCS (Eng and Edin). Laparoscopic vs Conventional Autopsy - A Promising Perspective. Arch Surg 1995;130:407–9.
[18] R.N. Cacchione, P. Sayad, A.M. Pecoraro, G.S. Ferzli, Laparoscopic autopsies, Surg. Endosc. 15 (6) (2001), 619-22.
[19] Fan J.T., D.K.H.; Poon, J.T.C.; Lo, O.S.H.; Beh, P.S.L.; Patil, N.G.; Law, W.L. Multimodality minimally invasive autopsy-A feasible and accurate approach to post-mortem examination. Forensic Science International, 2010, v 195 n 1–3, p 93–98. 2010.
[20] A. Schroeder, O. Mueller, S. Stocker, R. Salowsky, M. Leiber, M. Gassmann, et al., The RIN: an RNA integrity number for assigning integrity values to RNA measurements, BMC Mol. Biol. 7 (2006) 3.
[21] J.A. Cox, R.L. Lukande, S. Kalungi, E. Van Marck, K. Van de Vijver, A. Kambugu, et al., Needle autopsy to establish the cause of death in HIV-infected hospitalized adults in Uganda: a comparison to complete autopsy, J. Acquir Immune Defic. Syndr. 67 (2) (2014) 169–176.
[22] B.M. Blokker, A.C. Weustink, I.M. Wagensveld, J.H. von der Thusen, A. Pezzato, R. Dammers, et al., Conventional autopsy versus minimally invasive autopsy with postmortem MRI, CT, and CT-guided biopsy: comparison of diagnostic performance, Radiology 289 (3) (2018), 658-67.
[23] L.R. Massoth, N. Desai, A. Szabolcs, C.K. Harris, A. Neyaz, R. Crotty, et al., Comparison of RNA In Situ Hybridization and Immunohistochemistry Techniques for the Detection and Localization of SARS-CoV-2 in Human Tissues, Am. J. Surg. Pathol. 45 (1) (2021) 14–24.
[24] A. Farrugia, C. Keyser, C. Hollard, J.S. Raul, J. Muller, B. Ludes, Targeted next generation sequencing application in cardiac channelopathies: Analysis of a cohort of autopsy-negative sudden unexplained deaths, Forensic Sci. Int 254 (2015) 5–11.
[25] A. Farrugia, C. Keyser, B. Ludes, Detection of genetic variation in KCNQ1 gene by high-resolution melting analysis in a prospective-based series of postmortem negative sudden death: comparison of results obtained in fresh frozen and formalin-fixed paraffin-embedded tissues, Int J. Leg. Med 126 (4) (2012) 649–657.
[26] D. Wichmann, J.P. Sperhake, M. Lutgehetmann, S. Steurer, C. Edler, A. Heinemann, et al., Autopsy findings and venous thromboembolism in patients with COVID-19: a prospective cohort study, Ann. Intern. Med. 173 (4) (2020), 268-77.