Abdominal Radiology

© Springer Science+Business Media, LLC, part of Springer Nature 2018
Published online: 21 July 2018

Abdom Radiol (2019) 44:2074–2080
https://doi.org/10.1007/s00261-018-1702-1

Tissue sampling in the era of precision medicine: comparison of percutaneous biopsies performed for clinical trials or tumor genomics versus routine clinical care

Anjuli R. Cherukuri,[1] Meghan G. Lubner,[1] Ryan Zea,[2] J. Louis Hinshaw,[1] Sam J. Lubner,[3] Kristina A. Matkowskyj,[4] Marcia L. Foltz,[1] and Perry J. Pickhardt[1]

[1]Departments of Radiology, University of Wisconsin School of Medicine and Public Health, E3/311 Clinical Sciences Center, 600 Highland Ave, Madison, WI 53792, USA
[2]Biostatistics, University of Wisconsin School of Medicine and Public Health, E3/311 Clinical Sciences Center, 600 Highland Ave, Madison, WI 53792, USA
[3]Internal Medicine – Division of Human Oncology, University of Wisconsin School of Medicine and Public Health, E3/311 Clinical Sciences Center, 600 Highland Ave, Madison, WI 53792, USA
[4]Pathology and Lab Medicine, University of Wisconsin School of Medicine and Public Health, E3/311 Clinical Sciences Center, 600 Highland Ave, Madison, WI 53792, USA

Abstract

Purpose: The purpose of the study was to determine if patients undergoing percutaneous biopsy for genetic profiling are undergoing more biopsies (procedures, passes per procedure), or experiencing more procedure-related complications.
Methods: 60 patients undergoing biopsy procedures for genetic profiling were retrospectively compared with 60 consecutive control patients undergoing routine biopsies. Procedural details and related complications were collected. Results were analyzed using t-tests and logistic regression.
Results: Biopsied organs included mainly lung (n = 31), liver (n = 50), and lymph nodes (n = 18). The average number of core biopsy passes was 3.45 in the study group and 2.18 in the control group (0.73, 1.81; p = 0.0001). The average study patient underwent 1.44 biopsy procedures by radiology from 2016 to 2017, whereas the average control patient underwent 1.08 (0.1657, 0.5010, p = 0.0002). Results were similar when looking at the subset of patients undergoing liver biopsies. In our cohort of 120 patients total, only 6 complications were noted. There were 4 complications in the control patients and 2 complications in the study patients, all of which were pneumothoraces in patients undergoing lung biopsy; only 2 of these required treatment. The odds ratio for a complication occurring from an increase in one core biopsy is 1.07 (0.601, 1.573; p = 0.775), suggesting no significant relationship among the number of biopsies taken and the probability of complication in this cohort.
Conclusions: Patients being biopsied for genetic profiling or clinical study enrollment are undergoing more biopsy procedures and more biopsy passes per procedure, but are not experiencing a detectable increased rate of complications in this small cohort, single-center study.

Key words: Percutaneous—Biopsy—Genetics—Complications

Correspondence to: Meghan G. Lubner; *email:* mlubner@uwhealth.org

The last decade has seen a remarkable proliferation of treatment options for cancer. Nearly all the novel therapeutics have been a direct result of improvements in understanding of cancer biology. A critical component of these breakthroughs has been the ability to extract information about the tumor genome, and target variants unique to the cancer. In order to assay for genomic information using next generation sequencing (NGS), larger volumes of tissue may be required and are often obtained with percutaneous biopsy [1–5]. Percutaneous image-guided biopsies have a track-record of being relatively safe, minimally invasive procedures [6]. However,

Table 1. Organ/site biopsied in each cohort

Organ/site biopsied	Study group	Control group
Liver	25	25
Lung	20	11
Lymph node	10	8
Omentum/peritoneum	2	5
Adrenal	1	3
Body wall	0	3
Muscle	1	1
Ovary	1	0
Left upper quadrant	0	1
Paraspinal	0	1
Mediastinal	0	1
Retroperitoneal	0	1
Total	60	60

Table 2. Biopsy procedures, passes, and complications in all patients

	Study patients	Control patients	*p* value
Average biopsy procedures	1.42	1.08	0.0002
Average core biopsy passes	3.45	2.18	0.0001
Average total passes (with FNA)	3.97	2.25	< 0.0001
Number of complications	2	4	N/A

as with any intervention, there are risks for complications, which may vary with the site of biopsy. Depending on the site biopsied, bleeding is perhaps the most commonly encountered [7], with significant bleeding rates reported $< 2\%$ in most series [6, 8–10]. Percutaneous biopsy is a delicate balance of obtaining enough but not too much tissue from the safest possible site, at once optimizing diagnostic yield and minimizing risk of complications. If a higher risk biopsy is going to be performed, it is important for all parties to feel that the potential risk is outweighed by the potential benefit. It is logical to question whether adding ancillary next generation sequencing, which often requires more tumor-rich material with higher numbers of viable tumor cells [11] to routine pathological analysis leads to more passes per biopsy or more biopsy procedures per patent, and in turn whether obtaining additional tissue or larger cores may put these patients at increased risk of procedure-related complications. On balance, these potential risks are mitigated by dramatic improvements in survival with targeted agents, many of which are better tolerated than cytotoxic chemotherapy.

While many of these targeted agents have become a routine part of clinical care, new therapies continue to emerge along with a growing number of clinical trials that require additional tissue sampling as part of their eligibility assessment and enrollment requirements. The increase in clinical and research demand for core biopsy specimens and the need for more intensive testing on specimens obtained may also contribute to the potential need for more passes taken per biopsy procedure or more biopsy procedures performed in a single patient compared with those not enrolled in clinical trials.

As radiologists are being asked to do more image-guided biopsies for the purpose of genetic analysis or study enrollment, it would be helpful for both radiologists and patients to have a better understanding of the associated risks involved in order to proceed with truly informed consent. It is unclear whether study patients are definitively having more tissue obtained, and if yes, whether taking more tissue puts the patients at increased risk for procedure-related complications. The alternative to performing these biopsies would be to limit the number of passes to what the operator deems safe and use the tissue in a prioritized manner. The purpose of this study was to determine whether patients undergoing NGS or enrolled in clinical trials undergo more passes per biopsy procedure and biopsy procedures overall and if yes, to determine if a reasonable safety profile is maintained in these patients.

Methods

A retrospective, cohort study was performed comparing patients undergoing percutaneous biopsy procedures for the purpose of genetic profiling or clinical trial enrollment with control patients undergoing routine percutaneous biopsies for histopathologic analysis in a single institution.

Patient selection

A total of 60 consecutive patients being biopsied for NGS or enrollment in a clinical trial were collected from a 1-year period (November 2016–November 2017) from QA tracking databases for CT and US-guided biopsies. Imaging modality used for guidance is based on radiologist screening and biopsy site. Ultrasound is utilized for almost all solid organ, mesenteric/peritoneal masses, and for pleural-based lung masses in this cohort [12]. CT is generally used for deeper lung masses, adrenal masses, retroperitoneal lymph nodes, and occasionally deep pelvic targets not amenable to US-guided biopsy. These patients were identified as study patients on the intake form filled out by the radiology nursing staff, where the reason for the biopsy included enrollment for a clinical trial or additional genetic testing. This was confirmed based on clinical notes and orders in the electronic medical record. 60 consecutive routine patients undergoing biopsy for diagnosis were then collected from a similar time period (April 2017–November 2017). Since there were no genetic testing or trials that required renal biopsies at our institution, renal biopsies were excluded from the control group as well. Otherwise, all remaining organs and sites were included. Since this study was

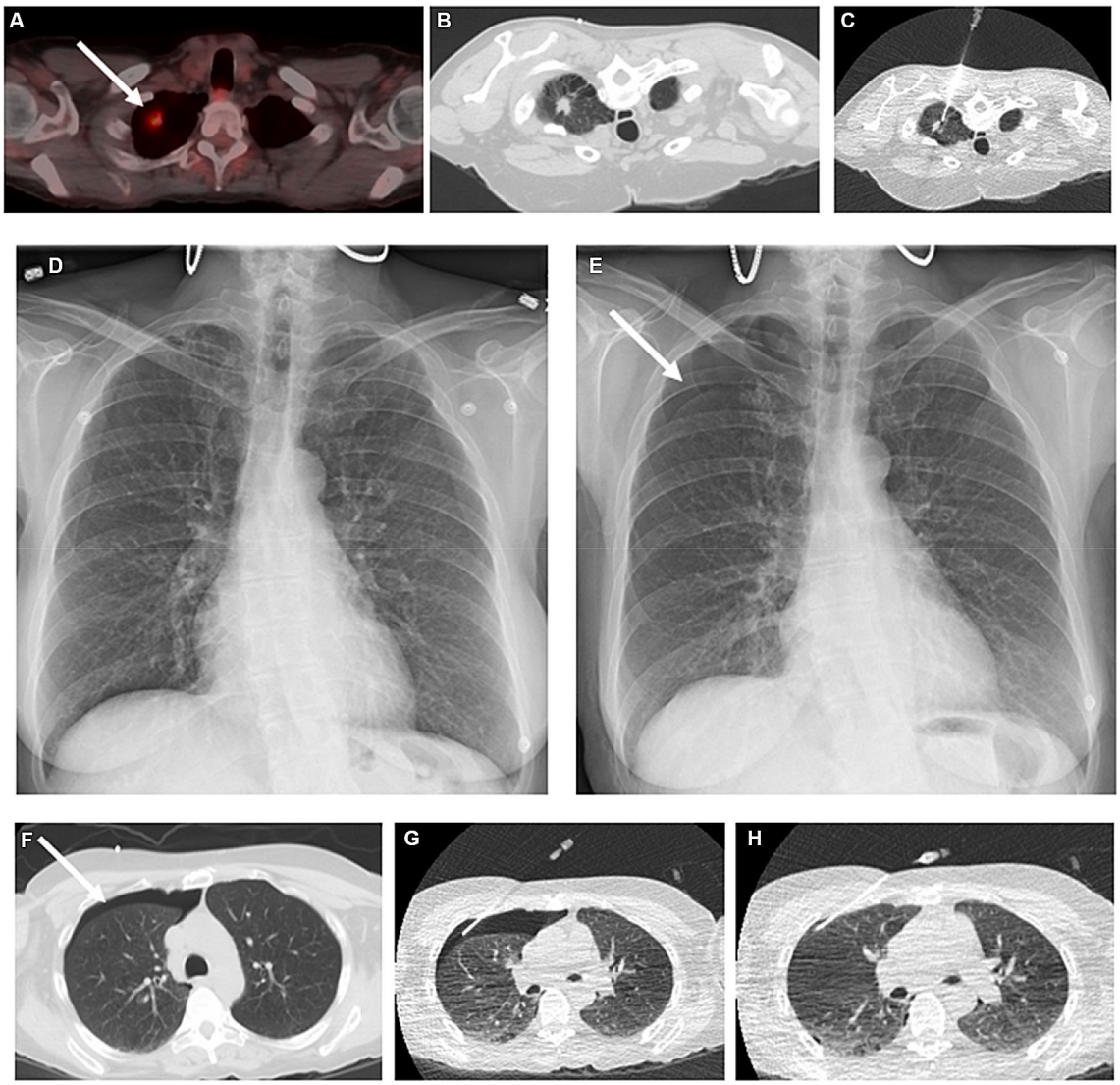

Fig. 1. 57-year-old female with spiculated FDG-avid RUL nodule seen on PET (arrow, **A**). Patient was placed in a prone position for CT-guided biopsy (**B**) which was performed with CT fluoroscopy using a co-axial technique using a 19-gauge introducer needle (**C**). A total of 3 core biopsy passes were taken using a 20-gauge, 1.2-cm throw core needle. Initial post-procedure chest X-ray demonstrated no pneumothorax (**D**). However, as the patient was leaving the department after 3 hours of observation, she developed chest heaviness. Repeat chest X-ray (**E**) demonstrated a small to moderate pneumothorax. Given the interval growth and patient symptoms, the patient was taken to the CT scanner and the pneumothorax localized for treatment purposes (CT, **F**). It was treated with placement of a 5 French Yueh centesis catheter (**G**), evacuation of the pneumothorax (**H**) and placement of a 60 cc autologous blood patch. A small apical pneumothorax persisted but was asymptomatic and remained stable over serial chest X-rays, and therefore, the patient was discharged without further treatment. This patient was in the control group.

performed in an adult hospital, all patients were 18 years or older, ranging from 18 to 84 (children were excluded).

Biopsy procedural details

At our facility, patients generally should have platelets $> 25{,}000$/mcL and an INR < 2.0 to proceed with percutaneous biopsy of non-superficial sites. This is slightly less conservative than the JVIR 2012 consensus guidelines [13]. CT-guided biopsies are performed using CT fluoroscopy with a co-axial technique utilizing a 19-g introducer needle with 20-gauge biopsy device in the lungs. Autologous parenchymal and pleural blood patches are routinely administered for lung biopsies [14, 15]. For CT-guided procedures in the mediastinum, retroperitoneum, or pelvis, a co-axial technique utilizing a 17-g introducer and 18-g core biopsy device is most commonly performed. Ultrasound-guided core needle

Table 3. Biopsy procedures, passes, and complications in liver subset of patients

	Study patients (liver only)	Control patients (liver only)	*p* value
Average biopsy procedures	1.40	1.08	0.0194
Average core biopsy passes	2.92	2.00	0.0174
Number of complications	0	0	N/A

biopsies are performed using a non-coaxial technique with an 18-gauge spring-loaded adjustable throw core biopsy device in most cases. A standardized two-person technique (sonographer and radiologist) as well as biopsy guides were utilized to maximize safety and yield in ultrasound-guided biopsies. The number of biopsy passes required varied with the clinical trial and desired pathologic test and was ultimately determined by the radiologist after taking patient safety and apparent tissue yield into account. Because of this standardized technique, common inclusion of trainees in biopsy procedures and due to prior institutional results showing little effect of radiologist experience, this was not tracked or assessed in this study [16].

Data collection

Data were collected from the biopsy intake data sheets, the biopsy QA databases, the electronic medical record (Epic, Verona, WI), and PACS (McKesson, San Francisco CA). Data collected included patient age, gender, weight, biopsy procedures in radiology in the current and preceding year, procedure type and site, number of passes, needle gauge, surgical pathology results, genetic/clinical study results, blood thinning medication use, INR, platelets, inpatient vs. outpatient status, admission following biopsy, additional imaging required post-biopsy, complications, and treatment of complications. In our institution, patients are routinely called the day following the procedure to screen for late complications. Complications were classified according to the Clavien–Dindo system [17].

Statistical analysis

To analyze the statistical significance of whether or not complications arise from study patients receiving more biopsies, a few tests were performed. First, a standard t-test was performed to check if the differences in the number of biopsies are indeed statistically significantly different between study and standard of care patients. Next, logistic regressions were performed comparing whether or not complications are associated with (1) the number of biopsies and (2) the interaction between the number of biopsies and patient type, expressed as Odds ratios. The test from (1) will show whether or not an increase in biopsies are related to an increase in complications, regardless of study status. The test from (2) will show whether an increase in biopsies are related to an increase in complications taking into account the study status. All tests were performed for core biopsies and the combination of core and FNA biopsies. FNA alone was not evaluated due to the small number.

Results

A total of 60 patients (31 men, 29 women; mean age, 60 years) were biopsied in the study group, and compared to 60 consecutive routine standard of care biopsy patients (28 men, 32 women; mean age, 57 years). Biopsied organs included mainly lung, liver, lymph nodes, and omentum, with assorted other organs including adrenal, muscle, ovary, and body wall masses (Table 1). The average number of core passes taken was 3.45 (range 1–12, median 3, SD 1.55) in the study group and 2.18 (range 0–4, median 2, SD 0.82) in the control group (0.73, 1.81; $p = 0.0001$). The average number total passes (core and FNA) was 3.97 in the study group and 2.25 in the control group (1.0463, 2.3871; $p < 0.0001$). The average study patient underwent 1.44 biopsy procedures (range 1–3, median 1, SD 0.59) by radiology from 2016 to 2017, whereas the average control patient underwent 1.08 (range 1–2, median 1, SD 0.28) over the same time period (0.1657, 0.5010, $p = 0.0002$) (Table 2).

Overall, complication rates were low in our cohort of 120 patients total with a total of 6 complications, all of which were pneumothoraces. 2 trace pneumothoraces occurred in the study patients that remained stable with no intervention needed (Clavien Dindo grade I). 4 small pneumothoraces occurred in the control patients, one of which required the patient to return to CT for a pleural blood patch [15] (Clavien Dindo grade IIIa) (Fig. 1), and another of which required admission to an outside facility with chest tube placement after their pneumothorax increased in size following discharge from our facility (Clavien Dindo grade IIIa).

When looking at a subset of patients who underwent liver biopsy (25 in the study group, 25 in the control group) and comparing study patients to control patients, the average number of cores were 2.92 and 2.00 (0.156, 1.684; $p = 0.0194$) and the average number of biopsy procedures were 1.40 and 1.08 (0.060, 0.580; $p = 0.0174$), respectively (Table 3). This is a similar trend to the general cohort. Because a co-axial technique was not used, and the capsule was punctured with each pass, it was felt that this subgroup may be at higher risk to develop more complications with more passes. However, no complications were seen in either the study or control sub-cohort of liver biopsy patients.

Of the 60 study patients, 53 patients had diagnostic genetic results and 7 had insufficient samples. Of the 7

Table 4. Examples of improvements in survival with targeted therapy

Diagnosis	Target	Median survival (PFS or OS) with targeted therapy	Median survival (PFS or OS) with chemotherapy alone	References
NSCLC	EGFR L858R	13.1 (PFS) mo	4.6 (PFS) mo	Zhou et al. [22]
NSCLC	ALK rearrangement	10.9 (PFS) mo	7.0 (PFS) mo	Solomon et al. [23]
Melanoma	BRAF V600E	15.9 (OS) mo	6–10 mo (historical control)	Sosman et al. [24]
Gastroesophageal	Her-2 Neu	13.8 (OS) mo	11.1 (OS) mo	Bang et al. [25]
Colorectal	RAS WT	28.4 (OS) mo	20.2 (OS) mo	Van Cutsem et al. [26]

patients with insufficient samples, 2 had insufficient viable nucleated cells for the study but with adequate tissue for pathologic diagnosis, 3 had inadequate cells for genetic testing but were not sent for routine pathologic diagnosis, 1 had insufficient tissue for either genetics or standard pathology, and 1 was necrotic with no usable tissue. Of the 60 control patients, 59 had diagnostic results. One core biopsy sample was originally reported as fibroconnective tissue, but after surgical resection proved to be liposarcoma.

Logistic regression and construction of univariate models expressed in terms of odds ratios were used to analyze the complication rates given their low occurrence. The odds ratio from an increase in one core biopsy is 1.07 (0.601, 1.573; $p = 0.775$), which is not statistically significant. Looking at the results of this model suggests that the odds ratio is near 1 with large, overlapping confidence intervals. This suggests that this study shows there is no relationship among the number of biopsies taken and the probability of complication in this cohort. The low number of events may certainly have caused this relationship.

Discussion

In an age of molecularly tailored oncologic therapies, pathologists are requiring more tissue to appropriately classify tumors and perform additional testing to determine treatment selection. While the increased volume of tissue or increased number of biopsies may seem excessive, the improvements in oncologic outcomes are highly significant, as outlined in Table 4. From a systems perspective, the converse is equally important; an absence of a molecular target suggests that clinicians should not expect any benefit from use of expensive targeted agents. Because of these demonstrable improvements in survival, early assessment of potential molecular targets is now included in treatment recommendations for lung cancer [18], colorectal cancer [19], gastroesophageal cancer [20], and melanoma [21]. New recommendations are emerging as rapidly as new targets and therapies are developed.

From a procedural perspective, the increased number of passes may put the patients at risk for increased complications, especially in organs like the liver where additional passes cause additional punctures through the liver capsule when co-axial technique is not used. Some studies have found significantly more complications with more passes but there is not universal consensus on this point [9, 27–31]. Therefore, this has not yet become a routine part of the informed consent discussion, or the assertions made around this potential concern are relatively vague, given a lack of concrete data on this topic to date. In this pilot study, we found that patients undergoing biopsies for the purpose of genetic profiling or clinical study enrollment are indeed undergoing more total biopsy procedures and more biopsy passes per biopsy procedure compared to control patients at our institution. Despite this, they are not experiencing complications at egregiously increased rates compared to those undergoing biopsies for routine diagnosis. Although this was a heterogeneous group of consecutive patients with biopsies at a variety of sites, the cohorts were fairly well matched overall, and the dominant biopsy sites in both groups were lung and liver. A co-axial technique is used in the lung for CT-guided procedures. As such, taking additional biopsy passes would increase needle dwell time but usually did not entail additional pleural punctures. However, we are increasingly utilizing US for pulmonary parenchymal masses that contact the pleura [12] and in these cases, co-axial technique is not used and each additional pass requires an additional pleural puncture. Small pneumothoraces are a common complication at CT-guided lung biopsy, and was seen in both our study and control cohorts, similar to results from a recent study [4]. In lung biopsies specifically, pneumothorax is the most frequent complication with rates ranging from 17 to 42.3% [32–35]. Chest tube placement is performed in 1–14.2% of patients who have a pneumothorax [32–35]. Pulmonary hemorrhage is reported in 4–27% [32, 34]. Of note, in our series, only one case of pneumothorax required chest tube placement. In the liver sub-cohort, where each new pass requires a new puncture of the liver capsule and risk for complication related to increased number of passes could in theory be highest, there were no complications identified in either group. Specifically, there was not an increased number of complications in the study group.

However, the complication rate in liver biopsies is generally low, reported between 0.5 and 3.3% [9, 36].

As noted above, complications related to percutaneous biopsy are relatively uncommon. These initial findings suggest that the small but statistically significant increase in number of passes and biopsy procedures do not seem to be directly or proportionally correlated to a marked increase in complications. At the very least, it suggests that we are not putting our patients at significantly increased risk, which can provide reassurance when discussing these procedures with patients and allow for more a more evidence-based informed consent process in these situations. However, this certainly warrants continued surveillance and/or a larger-scale study to confirm these preliminary results since an increasing number of biopsies are now being performed for genetic purposes.

Another issue raised is that even a routine standard of care biopsy for diagnosis now entails more intensive pathologic testing to fully characterize the tumor. For many tumors, immunohistochemistry and sometimes molecular testing are performed as part of the diagnosis, both in the primary and metastatic setting, independent of clinical trial enrollment. For example, at our institution, for a first time diagnosis of advanced lung cancer, after the biopsy is processed a hematoxylin and eosin (H&E)-stained slide is created to review the histology. Immunohistochemistry may be performed to classify the lesion as a non-small cell lung cancer (NSCLC) such as adenocarcinoma or squamous cell carcinoma or as a small cell carcinoma. In the setting of an adenocarcinoma diagnosis, additional staining for PD-L1 will be performed by immunohistochemistry, along with an in-house molecular and gene rearrangement panel. From a radiologist's perspective, the lung is a higher risk biopsy site and we tend to take smaller cores (20 gauge rather than 18 gauge in many cases) and potentially take fewer passes. This creates a disconnect between the amount of tissue obtained and the amount of tissue needed and increases the likelihood that the patient may need an additional biopsy procedure. This can lead to lower diagnostic yield of NGS [4]. This is even more problematic in the setting of unknown primary tumor where multiple immunohistochemical stains are likely to be performed in order to identify the origin of the neoplasm. In these cases, there may not be sufficient tissue to perform the additional required studies (estrogen receptor, progesterone receptor, Her-2, PD-L1 I, mismatch repair protein immunohistochemistry, etc) for patient treatment and thus there is no tissue available for next generation sequencing. It may be that we need to change our mindset and obtain more tissue from a standard of care biopsy that could potentially be used for downstream testing and obviate the need for future biopsies. Rather than obtaining 1–2 cores for most biopsies, where safe, it may be useful to obtain 3–4 cores. Again, it is a delicate balance of obtaining enough tissue without putting the patient through unnecessary additional passes, which can change on a case by case basis, depending on the clinical scenario, site of biopsy, and targeted lesion characteristics. In addition, when choosing a site for biopsy, we need to keep these considerations in mind [4].

In the cases where material was not sufficient for genetic testing, necrosis was a common problem. To enable genetic testing, it is important to choose a site and a portion of the selected target with viable tumor if at all possible. PET as well as other imaging features such as enhancement or color Doppler flow may be helpful in targeting.

Limitations of this study that could be addressed on future projects include low patient numbers for the complication rate and the retrospective nature. The low patient numbers contributed to the low number of complications (which are uncommon at many sites) and possibly the inability to detect an increase in complication rates in the study group. However, this is meant to be a pilot study and a larger multi-center investigation is warranted. In addition, our review included an assortment of organs and sites. Future studies with larger cohorts could more directly compare specific sites, such as lung, where our complication rate was the greatest and other studies have shown to be the most biopsied organ for genetic purposes at 36% [4]. Our institution is continuing to track patients for future review.

Conclusions

In summary, while patients being biopsied for the purpose of genetic profiling or clinical study enrollment are undergoing more biopsy procedures and biopsy passes per procedure, they are not experiencing a detectable increased rate of complications, in this small cohort, single institution experience.

Compliance with ethical standards

Funding None.

Disclosures Dr. Lubner has no relevant conflicts, but receives Grant funding from Philips, Ethicon. Dr. Pickhardt has no relevant conflicts but is co-founder of VirtuoCTC, consultant for Bracco and Check-Cap, and shareholder in SHINE, Elucent, and Cellectar Biosciences. Dr. Hinshaw has no relevant conflicts but is a consultant for Neuwave, Shareholder in Elucent, LiteRay, Accure, Histosonics, and Cellectar. All other authors have no disclosures.

Research approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study, formal consent is not required.

References

1. Corr BR, Behbakht K, Spillman MA (2013) Gynecologic biopsy for molecular profiling: a review for the interventional radiologist. Semin Intervent Radiol 30:417–424
2. Cox VL, Bhosale P, Varadhachary GR, et al. (2017) Cancer genomics and important oncologic mutations: a contemporary guide for body imagers. Radiology 283:314–340
3. MacConaill LE (2013) Existing and emerging technologies for tumor genomic profiling. J Clin Oncol 31:1815–1824
4. Sabir SH, Krishnamurthy S, Gupta S, et al. (2017) Characteristics of percutaneous core biopsies adequate for next generation genomic sequencing. PLoS One 12:e0189651
5. Basik M, Aguilar-Mahecha A, Rousseau C, et al. (2013) Biopsies: next-generation biospecimens for tailoring therapy. Nat Rev Clin Oncol 10:437–450
6. Winter TC, Lee FT Jr, Hinshaw JL (2008) Ultrasound-guided biopsies in the abdomen and pelvis. Ultrasound Q 24:45–68
7. Kennedy SA, Milovanovic L, Midia M (2015) Major bleeding after percutaneous image-guided biopsies: frequency, predictors, and periprocedural management. Semin Intervent Radiol 32:26–33
8. van Beek D, Funaki B (2013) Hemorrhage as a complication of percutaneous liver biopsy. Semin Intervent Radiol 30:413–416
9. Atwell TD, Smith RL, Hesley GK, et al. (2010) Incidence of bleeding after 15,181 percutaneous biopsies and the role of aspirin. AJR Am J Roentgenol 194:784–789
10. Pieper M, Schmitz J, McBane R, et al. (2017) Bleeding complications following image-guided percutaneous biopsies in patients taking clopidogrel-a retrospective review. J Vasc Interv Radiol 28:88–93
11. Biankin AV, Waddell N, Kassahn KS, et al. (2012) Pancreatic cancer genomes reveal aberrations in axon guidance pathway genes. Nature 491:399–405
12. Lee MH, Lubner MG, Hinshaw JL, Pickhardt PJ (2018) Ultrasound guidance versus CT guidance for peripheral lung biopsy: performance according to lesion size and pleural contact. AJR Am J Roentgenol 210:W1–W8
13. Patel IJ, Davidson JC, Nikolic B, et al. (2012) Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions. J Vasc Interv Radiol 23:727–736
14. Graffy P, Loomis SB, Pickhardt PJ, et al. (2017) Pulmonary intraparenchymal blood patching decreases the rate of pneumothorax-related complications following percutaneous CT-guided needle biopsy. J Vasc Interv Radiol 28(608–613):e601
15. Wagner JM, Hinshaw JL, Lubner MG, et al. (2011) CT-guided lung biopsies: pleural blood patching reduces the rate of chest tube placement for postbiopsy pneumothorax. AJR Am J Roentgenol 197:783–788
16. Prince J, Bultman E, Hinshaw L, et al. (2015) Patient and tumor characteristics can predict nondiagnostic renal mass biopsy findings. J Urol 193:1899–1904
17. Dindo D, Demartines N, Clavien P (2004) Classification of surgical complications. Ann Surg 240:205–213
18. Ettinger DS, Wood DE, Aisner DL, et al. (2017) Non-small cell lung cancer, version 5.2017 clinical practice guidelines in oncology. J Natl Compr Canc Netw 15:504–535
19. Benson AB, Venook AP, Cederquist L, et al. (2017) Colon cancer, version 1.2017 clinical practice guidelines in oncology. J Natl Compr Cancer Netw 15:370–398
20. Ajani JA, D'Amico TA, Almhanna K, et al. (2016) Gastric cancer, version 3.2016. J Natl Compr Cancer Netw 14:1286–1312
21. Coit DG, Thompson JA, Algazi A, et al. (2016) Melanoma, version 2.2016. J Natl Compr Cancer Netw 14:450
22. Zhou C, Wu YL, Chen G, et al. (2011) Erlotinib versus chemotherapy as first-line treatment for patients with advanced EGFR mutation-positive non-small-cell lung cancer (OPTIMAL, CTONG-0802): a multicentre, open-label, randomised, phase 3 study. Lancet Oncol 12:735–742
23. Solomon BJ, Mok T, Kim DW, et al. (2014) First-line crizotinib versus chemotherapy in ALK-positive lung cancer. N Engl J Med 371:2167–2177
24. Sosman JA, Kim KB, Schuchter L, et al. (2012) Survival in BRAF V600-mutant advanced melanoma treated with vemurafenib. N Engl J Med 366:707–714
25. Bang YJ, Van Cutsem E, Feyereislova A, et al. (2010) Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet 376:687–697
26. Van Cutsem E, Lenz HJ, Kohne CH, et al. (2015) Fluorouracil, leucovorin, and irinotecan plus cetuximab treatment and RAS mutations in colorectal cancer. J Clin Oncol 33:692–700
27. Cohen MB, A-Kader HH, Lambers D, Heubi JE (1992) Complications of percutaneous liver biopsy in children. Gastroenterology 102:629–632
28. Seeff LB, Everson GT, Morgan TR, et al. (2010) Complication rate of percutaneous liver biopsies among persons with advanced chronic liver disease in the HALT-C trial. Clin Gastroenterol Hepatol 8:877–883
29. Heng C, Hansen BE, Tang WY, et al. (2017) Multiple biopsy passes and the risk of complications of percutaneous liver biopsy. Eur J Gastroenterol Hepatol 29:36–41
30. McGill DB, Rakela J, Zinsmeister AR, Ott BJ (1990) A 21-year experience with major hemorrhage after percutaneous liver biopsy. Gastroenterology 99:1396–1400
31. Abel EJ, Heckman JE, Hinshaw L, et al. (2015) Multi-quadrant biopsy technique improves diagnostic ability in large heterogeneous renal masses. J Urol 194:886–891
32. Winokur RS, Pua BB, Sullivan BW, Madoff DC (2013) Percutaneous lung biopsy: technique, efficacy, and complications. Semin Intervent Radiol 30:121–127
33. McSweeney SE, O'Regan KN, Mc Laughlin PD, Crush L, Maher MM (2012) Evaluation of the efficacy and safety of percutaneous biopsy of lung. Open Respir Med J 6:82–88
34. Wu CC, Maher MM, Shepard JA (2011) Complications of CT-guided percutaneous needle biopsy of the chest: prevention and management. AJR Am J Roentgenol 196:W678–682
35. Hiraki T, Mimura H, Gobara H, et al. (2010) Incidence of and risk factors for pneumothorax and chest tube placement after CT fluoroscopy-guided percutaneous lung biopsy: retrospective analysis of the procedures conducted over a 9-year period. AJR Am J Roentgenol 194:809–814
36. McInnes MDF, Kielar AZ, Macdonald DB (2011) Percutaneous image-guided biopsy of the spleen: systematic review and meta-analysis of the complication rate and diagnostic accuracy. Radiology 260:699–708