10.1148/radiol.2018181140

Appendix E1

Registration

Enrolled participants were registered through Protocol Participant Registration Office. Excluded participants and reasons for exclusion were recorded in our study database (Table E2).

Registered participants were randomized electronically in a 1:1 ratio using permuted blocks of random size. The randomization result was saved in the electronic scheduling system available to IR staff on the day of biopsy. Since the 2 techniques being evaluated were entirely unique (one requiring a blood draw and the other using a mechanical device), it was not possible to conduct a blinded study for either IR staff or participants.

Procedures

Biopsies and postprocedural care were performed as per our standard practice. All participants were consented for biopsy either at the time of outpatient clinic visit or on the day of biopsy. Moderate sedation using intravenous midazolam and fentanyl was used for all participants. Noncontrast enhanced computed tomography and CT-fluoroscopy were used for imaging guidance (Axial plane, 5 mm slice thickness, 1.375:1 pitch, 60 milliamperage. INTERACT Discovery RT. GE Healthcare, Chalfont St Giles, UK). A limited CT scan of the lesion and adjacent lung parenchyma was acquired for biopsy planning. A sterile field was set up at the planned needle entry point. For the ABPI arm, at the start of the procedure, phlebotomy was performed, drawing 2–3 mL of the participant's blood into a labeled anticoagulant-free syringe which was capped and kept in a cap-down position. Biopsies were performed coaxially using a 19-gauge introducer needle. Angiotech needle was mandatory for hydrogel plug arm but ABPI arm could be done using any 19-gauge needle at the discretion of the interventional radiologist. Core and/or fine needle biopsy (FNB) samples were obtained using 20-gauge semiautomatic spring-loaded core biopsy needle (Temno ACT or Temno Evolution, CareFusion, Vernon Hills, IL. or Bard Mission, Bard Peripheral Vascular, Inc. Tempe, AZ) or 20–22-gauge FNB needle (Westcott, BD Medical, Franklin Lakes, NJ). A cytotechnologist and an attending cytopathologist performed preliminary examination of the samples to assess adequacy. The interventional radiologist took as many samples as needed and deemed safe. Once sampling was done, and prior to removal of the introducer needle, the appropriate sealant technique was deployed according to the randomization arm. If the participant was assigned to the ABPI arm, the introducer needle was pulled back in the lung parenchyma to 2–3 cm under the pleural surface, and the blood was injected steadily and slowly as the needle was pulled out of the lung (24) (Fig E1).

If the participant was assigned to hydrogel plug arm, distance from skin to pleura was measured over the needle on one of procedural images and the number was used in the device's deployment mechanism. The introducer needle hub was hydrated with saline, the hydrogel plug housing adapter was locked to the needle and after hydration of the hub of adapter with saline, the deployment device was mounted on the needle-adapter assembly and the plug was deployed as per manufacturer's user manual (Fig E2).

Standard post procedural CT images were obtained and participants were transferred to the recovery unit where at least two chest radiographs were obtained at 0 and 2 hours after the procedure. Additional radiographs were obtained if indicated.

Measurements

Pneumothorax was mainly defined based on post procedure chest radiographs. The investigator who performed the biopsy was in charge of determining pneumothorax as per our routine practice. They routinely consulted at least one other investigator for consensus about pneumothorax and its management. The chest radiograph and clinical findings were the main mechanisms for determining pneumothorax. Any discernible pneumothorax on chest x-rays was considered a positive finding (Fig E1). Any pneumothorax larger than miniscule on CT images was also considered a positive finding (Fig E2). To maintain impartiality, within 2 weeks of the biopsy, all chest radiographs were reviewed by one of three study interventional radiologists who was not involved with the biopsy procedure (MM, NM and SBS). All disagreements were resolved by consensus with all three of the above investigators reviewing the images. Biopsy data points including intraprocedural exclusions were captured by individual investigators performing biopsies through standardized reporting using a customized template and subsequently transferred to our study database. These data points were checked by two investigators (CZ and MI each with 2–4 years of experience) and discrepancies were reviewed by two investigators (MM and NM) for consensus.

Postbiopsy Care

Participants with no or small stable asymptomatic pneumothorax were discharged home. A chest tube was placed for participants with a symptomatic or enlarging pneumothorax. Participants who underwent chest tube placement were often admitted for overnight observation if they had a persistent air leak late in the day. Chest tube was removed when there was no longer an air leak and the pneumothorax did not recur after the chest tube was clamped for 2 hours. Participants were discharged home following chest tube removal. At the time of discharge all participants were instructed to call back with any symptoms and particularly chest pain and shortness of breath. In addition, participants who did not receive a chest tube received a phone call by one of outpatient clinic nurses within two weeks of the biopsy with a questionnaire designed to capture delayed pneumothorax. For participants that could not be reached, the incidence of a delayed pneumothorax was determined by chart review. If chart review was inconclusive, the participants were considered lost to follow-up for delayed pneumothorax.

Table E1: Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
• ≥ 18 years of age	• Potential study participant not interested
• IR referral for biopsy of lung lesion	• Planned path of needle through nonaerated lung***
• CT guidance	• Skin-to-pleura distance less than 1 cm*
• Target lesion of any size	• Skin-to-pleura distance more than 7 cm*
• Coaxial technique	• More than 1 biopsy target on the same side requiring more than 1 pleural puncture**
• Biopsy type: Core or fine-needle biopsy	• Prior ipsilateral pleura/lung interventions***
• Pleura-to-target distance equal or more than 1.5 cm based on the planned path of needle*	o Chest tube placement
• Skin-to-pleura distance 1–7 cm*	o Surgery

• Introducer needle size: 19 Gauge*	o Pleurodesis
• Introducer needle type: Angiotech*	o Radiation treatment
• Introducer needle length equal or less than 15 cm*	• Prior enrolment into this study****
• Planned needle path without transgression of fissure, bleb, or bulla**	

* Requirements for hydrogel plug device.

** Increases the risk of pneumothorax.

*** Lowers the risk of pneumothorax.

**** Creates statistical bias.

CT = Computed tomography, IR = Interventional radiology.

Table E2: Participants Excluded at Screening

Reason	*n* = 1598
Potential study participant not interested	396
Coaxial 19 Gauge technique not used	27
Needle through nonaerated lung	258
Needle through fissure or bulla	88
More than 1 biopsy target on same side	11
Pleura-to-target distance < 1.5 cm	467
Skin-to-pleura distance > 7 cm	7
Introducer needle length > 15 cm	2
Same participant for repeat biopsy	7
Prior ipsilateral lung/pleura interventions	
Surgery	247
Radiation	63
Chest tube	17
Pleurodesis	8

Table E3: Intraoperative Exclusion Criteria

Intraoperative exclusion criteria	*n* = 89
More than 1 needle pass through visceral pleura	17
Passage of needle through pleural fissure, bleb, or bulla	19
Passage of needle through consolidated or nonaerated lung	7
Pleura-to-target distance less than 1.5 cm	2
Skin-to-pleura distance more than 7 cm	6
Introducer needle length more than 15 cm	2
Coaxial technique not used	4
Development of pneumothorax before deployment of sealant	7
Use of introducer needle larger than 19 gauge	6
Operator forgot to deploy sealant	19

Table E4: Demographics of Study Participants

	Randomization Population (*n* = 453)		Modified Intent-to-Treat Population (*n* = 406)	
Characteristic	ABPI (*n* = 226)	Hydrogel plug (*n* = 227)	ABPI (*n* = 199)	Hydrogel plug (*n* = 207)
Age (Mean, Range)	66.8 (32–92)	67.0 (24–93)	66.3 (32–92)	66.9 (24–93)
Female	66.6 (32–92)	65.9 (27–93)	66.2 (32–92)	66.1 (27–93)
Male	66.9 (34–89)	68.5 (24–91)	66.4 (34–89)	67.9 (24–91)
Sex				
Female	124 (55%)	127 (56%)	113 (57%)	114 (55%)
Male	102 (45%)	100 (44%)	86 (43%)	93 (45%)
Race				
White	186 (82%)	189 (83%)	165 (83%)	171 (83%)
Black/African American	11 (5%)	10 (4%)	7 (4%)	10 (5%)
Asian/Pacific Islands	13 (6%)	12 (5%)	11 (6%)	12 (6%)
Other	2 (1%)	3 (1%)	2 (1%)	2 (1%)
Unknown	1 (0%)	1 (0%)	1 (1%)	1 (0%)
Refused to answer	13 (6%)	12 (5%)	13 (7%)	11 (5%)
Ethnicity				
Non-Hispanic	216 (96%)	217 (96%)	190 (95%)	198 (96%)
Hispanic	10 (4%)	10 (4%)	9 (5%)	9 (4%)

ABPI = Autologous blood patch injection.

Table E5: Length of Hospital Stay for Pneumothorax or Delayed Pneumothorax by Treatment Assignment

	ABPI	Hydrogel plug	*P*
Days of Hospital Stay for Pneumothorax within 2 hours	*n* = 42	*n* = 60	
Mean (SD)	1.6 (2.7)	0.80 (1.1)	0.03
0	22 (52%)	32 (53%)	
1	10 (24%)	16 (27%)	
2	2 (5%)	8 (13%)	
3	0 (0%)	1 (2%)	
4	0 (0%)	2 (3%)	
5	3 (7%)	1 (2%)	
6	2 (5%)	0 (0%)	
7	1 (2%)	0 (0%)	
10	2 (5%)	0 (0%)	
	ABPI	Hydrogel plug	
Days of Hospital Stay for Delayed Pneumothorax	*n* = 3	*n* = 3	
0	2 (67%)	1 (33%)	
1	1 (33%)	1 (33%)	
2	0 (0%)	1 (33%)	

Study participants with 0 length of stay were discharged the day of biopsy. ABPI = Autologous blood patch injection, SD = Standard deviation.