Appendix 1: Summary of studies evaluating thoracentesis-related complications in last 6 years

Author	Study type	Main finding	Overall risk estimate for consent
Pneumothorax			**<5%**
Cavanna 2014[1]	Retrospective cohort	Decreased risk of PTX with ultrasound guidance used for 445 cancer patients. 3.37% incidence of PTX, 0.97% with ultrasound guidance, 8.89% without.	
Perazzo 2014[2]	Prospective study	Decreased risk of PTX with ultrasound guidance (1.25% vs 12.5%)	
Ault 2015[3]	Prospective cohort	9,230 thoracenteses. 0.61% PTX rate; PTX associated with >1500ml removed, unilateral procedure, more than one pass through skin and low BMI (<18). 0.18% bleeding episodes, 0.01% RPO.	
Cho 2017[4]	Retrospective cohort	0.62% PTX rate. PTX associated with low BMI (<18.5)	
Shechtman 2020[5]	Retrospective cohort	12% PTX rate. PTX associated with higher rate of congestive heart failure, smaller depth of pleural fluid, larger volume of fluid drained and bilateral procedures.	
Touray 2017[6]	Retrospective cohort	Iatrogenic PTX rate 1.38% with use of ultrasound.	
Hooper 2015[7]	National Audit (BTS)	15/1162 (1.3%) patients developed an iatrogenic pneumothorax.	
Bleeding complications			**<1%**
Ault 2015[3]	Prospective study	0.18% bleeding complications, 0.01% haemothorax, 0.05% rate of haemothorax without correction of bleeding risk; no association of bleeding risk with patient or laboratory parameters.	
T Touray 2017[6]	Retrospective cohort	Bleeding complication rate 0.4%	
Perl 2020[8]	Retrospective case control	No increased bleeding risk in clopidogrel treated patients. 2.2% vs 1.2%	
Hooper 2015[7]	National Audit (BTS)	13/1162 (1.1%) patients developed a haemothorax and 12/1162 (1%) developed a chest wall haematoma.	
Re-expansion pulmonary oedema (RPO)			**<1%**
Ault 2015[3]	Prospective cohort	10/9320 (0.01%) incidence of RPO; association with volume of fluid removed and non-inflammatory conditions.	
Senitko 2019[9]	Prospective randomised study	Vacuum aspiration associated with increased risk of complications (5/51 vs 0/49 p=0.03), PTX n=3, surgically treated haemothorax and death (n=1), RPO causing respiratory failure (n=1)	
Failed procedure / dry tap			**4%**
Hooper 2015[7]	National Audit (BTS)	43/1162 (3.7%) had a failed procedure or dry tap.	
Pain			**5%**
Hooper 2015[7]	National Audit (BTS)	112/1162 (5%) developed pain.	
Symptomatic hypotension			**<1%**
Hooper 2015[7]	National Audit (BTS)	7/1162 (0.6%) developed symptomatic hypotension.	
Ault 2015[3]	Prospective cohort	6/9320 (0.1%) had a vasovagal reaction.	
Organ puncture			**<1%**
Hooper 2015[7]	National Audit (BTS)	3/1162 (0.3%) had an organ puncture.	
Ault 2015[3]	Prospective cohort	1/9320 (0.01%) splenic rupture.	

BMI, body mass index; PTX, pneumothorax; RPO, re-expansion pulmonary oedema

Appendix 2: Summary of the rates of different complications related to intercostal drains

Complication	Study type	Study details	Risk of complication per study	Overall risk estimate for consent
Immediate complications				
Pain				**8%**
Hooper 2015[7]	UK National Audit (BTS)	1394 procedures, 88% 6-16F intercostal drains.	8%	
Inappropriate placement				**1%** (small-bore drains) **6%** (large-bore drains)
Vilkki 2020[10]	Retrospective cohort	1169 procedures, more than half were small-bore drain insertions.	0.43%	
Hooper 2015[7]	UK National Audit (BTS)	See above	2%	
Kong 2014[11]	Retrospective cohort	1050 drain insertions for trauma patients, 32F or larger.	6%	
Maritz 2009[12]	Local audit at a tertiary hospital	273 drain insertions for trauma patients, no information on drain sizes.	6.9%	
Symptomatic hypotension				**2%**
Hooper 2015[7]	UK National Audit (BTS)	See above	1.9%	
Iatrogenic haemothorax				**<1%**
Jackson 2021[13]	Retrospective cohort	879 small-bore drain insertions.	0.1%	
Kong 2014[11]	Retrospective cohort	See above	0.2%	
Hooper 2015[7]	UK National Audit (BTS)	See above	1.3%	
Organ Puncture				**<1%**
Vilkki 2020[10]	Retrospective cohort	See above	0%	
Jackson 2021[13]	Retrospective cohort	See above	0%	
Kong 2014[11]	Retrospective cohort	See above	0.4%	
Hooper 2015[7]	UK National Audit (BTS)	See above	0.6%	

(delayed complications on next page)

Appendix 2: Summary of the rates of different complications related to intercostal drains (cont.d)

Complication	Study type	Study details	Risk of complication per study	Overall risk estimate for consent
Delayed complications				
Pain				**16%**
Hooper 2015[7]	UK National Audit (BTS)	See above	15.6%	
Drain blockage				**8%**
Hooper 2015[7]	UK National Audit (BTS)	See above	8.2%	
Drain displacement				**5%**
Kong 2014[11]	Retrospective cohort	See above	1.3%	
Jackson 2021[13]	Retrospective cohort	See above	3.9%	
Hooper 2015[7]	UK National Audit (BTS)	See above	9.2%	
Surgical emphysema				**5%**
Hooper 2015[7]	UK National Audit (BTS)	See above	4.2%	
Jackson 2021[13]	Retrospective cohort	See above	4.6%	
Skin infection				**1 %**
Hooper 2015[7]	UK National Audit (BTS)	See above	1%	
Re-expansion pulmonary oedema				**<1%**
Jackson 2021[13]	Retrospective cohort	See above	0%	
Hooper 2015[7]	UK National Audit (BTS)	See above	0.6%	
Pleural space infection				**<1%**
Jackson 2021[13]	Retrospective cohort	See above	0.4%	
Hooper 2015[7]	UK National Audit (BTS)	See above	0.4%	
Death				**<1%**
Kong 2014[11]	Retrospective cohort	See above	0%	
Jackson 2021[13]	Retrospective cohort	See above	0%	
Hooper 2015[7]	UK National Audit (BTS)	See above	0.1%	

Appendix 3: IPC-related complications, rates of occurrence and management

Complication	Outcomes	Risk of complication per study	Overall risk estimate for consent
Pain necessitating IPC removal			**<1%**
Asciak 2019[14] Tremblay 2006[15]	Severe or persistent pain should raise concern for intercostal nerve irritation, and IPC removal should be considered.	0.4% - 0.5%	
Pain towards the end of the drainage procedure			**Not quantified in literature, but commonly encountered in clinical practice**
	May indicate the presence of underlying non-expandable lung. Routine pre-drainage analgesia may help reduce discomfort, or a revised drainage protocol may be required, with less frequent or smaller volumes of fluid drainage.	Fairly common	
IPC-related infection			**5%**
Asciak 2019[14] Fysh 2013[16] Tremblay 2006[15]	IPC related pleural infections carry a 0.29% mortality rate, but the majority (94%) respond to antibiotics treatment. Some may require intravenous antibiotics and continuous IPC drainage (by attaching the IPC to an underwater seal).[16] The majority do not require the IPC to be removed.[17]	Superficial (cellulitis): 1.6% - 2.5% Pleural infection: 3.2% - 5%	
Non-draining septated IPC-related pleural effusion			**<15%**
Asciak 2019[18] Thomas 2015[19]	Treatment with intrapleural fibrinolytics. A small study showed a single dose of fibrinolytic agent (majority given 4-10 mg tissue plasminogen activator (TPA)) was associated with an increased volume of drainage and decreased symptoms but was also associated with a 3% risk of non-fatal pleural bleed.[19] There is a lack of robust data on the right treatment but often there is a lack of alternatives in patients who are not suitable candidates for surgery, thus intrapleural fibrinolytics can be considered in select patients.	4%-14%	
IPC blockage			**4%**
Van Meter 2011[20]	Usually due to fibrinous debris. A catheter flush with sterile saline often clears any catheter obstruction, however, fibrinolytic therapy (eg, 4 mg alteplase in 20 mL sterile saline instilled through the IPC (similar to the method used for central line unblocking), repeated a second time if inadequate drainage (<150 mL)), may be considered for more resistant occlusion, although this carries considerable cost and re-obstruction may occur.[21 22 23]	4%	
IPC fall out or dislodgement			**1%**
Tremblay 2006[15]	May require new IPC insertion if ongoing pleural effusion re-accumulation.	1%	

Appendix 4: LAT troubleshooting guidance

Situation	Potential approach
No fluid / small fluid volume in lateral decubitus position	It is common for fluid to "fall" away anteriorly and posteriorly with the patient lying on their side, thus it is advised that patients be scanned in clinic prior to listing for LAT to avoid this situation. However, if encountered, a per-patient decision needs to be made as to whether to: 1. Abandon the procedure (perhaps with a view to re-listing after further fluid accumulation), 2. Attempt an on-table induced pneumothorax (usually with direct US guidance of a needle into fluid), or 3. Proceed with a 'dry' LAT, whereby a careful surgical dissection method is used to access the pleural space and allow air to entrain. Recent data suggest 78% of UK LAT sites would induce a pneumothorax for LAT if needed.[24] As above, the procedure can be undertaken whilst on the table (with thoracic US to check for absence of sliding and seashore sign) or shortly prior to LAT (with a lateral decubitus CXR to check for sufficient lung collapse).
Inability to aspirate fluid during anaesthesia or collapse lung following blunt dissection	This situation is likely to occur when fluid is heavily loculated or septated, perhaps due to chronicity or infection, and may not be appreciable until pleural access is attempted on table. As above, a per-patient decision needs to be made to either: 1. Abandon the procedure with a view to considering alternative pleural biopsy techniques at a later date (eg, VATS or image-guided), or 2. Proceed to on-table US-guided parietal pleural biopsy.
Unable to advance trochar through rib space	This may occur in patients who have intrinsically narrow rib spaces or in those who have been positioned on the table in such a way as to promote 'rib crowding'. For the former, an alternative rib space/location may be required, although due consideration should be given to whether the likely risk of pain and/or injury to sub-costal structures may be excessive. In all cases, it may be possible to widen the chosen rib space by placing a folded pillow or blanket between the patient and the bed, creating a gentle convex arch in their spine.
Difficulty penetrating pleural layer (especially with trochar)	It is common for the dissection tract to collapse due to pressure from surrounding tissues, impeding passage of instruments. This is more likely to occur in larger or obese patients, in whom there may be a significant distance from the skin to the parietal pleural layer. This can be accurately measured using US prior to beginning dissection. However, this situation can usually be overcome by slow, methodical, repeated dissection along the same tract. However, this may increase the risk of pain, subsequent local surgical emphysema post procedure, and delayed tract healing.
Unable to visualise ribs on inspection	This is common in patients with significant or chronic pleural inflammation, fibrosis, or malignant infiltration. Using a rigid instrument (usually a 0-degree scope with closed biopsy forceps attached), it may be possible to press against the posterior thoracic wall and slide from side to side, thus allowing the operator to 'feel' where the rib spaces are. In rare circumstances, external transillumination may also be an option.
Unable to visualise posterior thoracic wall due to adhesions or loculations	In some instances of severe septation, it may be necessary to abandon the LAT ± convert to an on-table US-guided biopsy. However, if free-flowing fluid is present, it is usually possible to undertake careful, methodical dissection of adhesions and septations to create a tract to the posterior thoracic wall. This is typically done using a blunt instrument, such as closed biopsy forceps. Where feasible, electrocautery may also be considered but should only be used by those with adequate experience and training.
Pain during biopsies	The parietal pleural layer is highly innervated and thus a degree of discomfort during pleural biopsies is to be expected, with these occasionally being extremely painful. Direct application of local anaesthesia is usually impractical. If biopsies are limited by pain, then additional boluses of opiate (eg, fentanyl 25 µg) should be considered. Accordingly, care should be taken to ensure sufficient intravenous analgesia is available and that it can be administered by a non-sterile member of the team during LAT.

(continued on next page)

Appendix 4: LAT troubleshooting guidance (cont.d)

Situation	Potential approach
Vasovagal syncope during talc poudrage	This complication can arise due to severe pain, acute local inflammatory effects of talc or, with some aerosol talc preparations, cold gas hitting the pleural surface. Treatment is supportive and, although symptoms are usually transient, they may be extreme enough to require early termination of LAT to allow rapid drain insertion and for the patient to be nursed on their back. Occasionally, bolus intravenous fluids are required.
Suspected intercostal artery damage	This usually occurs because of biopsies and should prompt planned diagnostic and therapeutic treatments to be immediately abandoned in favour of emergency procedures. Intercostal artery laceration is usually visually distinct from the expected post-biopsy pleural ooze, which is typically self-limiting. As above, it is strongly endorsed that all LAT centres adopt a site-specific standardised protocol for management of this scenario and that this be prepared in line with local major haemorrhage pathways. Intercostal artery bleeds may also present post-LAT if laceration occurred during initial dissection but was concealed by the trochar causing tamponade during the procedure. As well as abandoning diagnostic procedures, actions should include: a) Application of external pressure over the suspected bleeding site. b) Insertion of at least two large-bore venous cannulas. c) Urgent venous sampling for full blood count, renal function, clotting screen, group and screen, and crossmatch (4 units). Venous blood gas analysis should also be performed to obtain immediate values for haemoglobin and lactate. d) Intravenous fluid resuscitation. e) Frequent, regular measurement of observations (pulse, blood pressure, respiratory rate, peripheral saturations) f) Insertion of large bore chest tube via LAT tract. g) Portable chest x-ray and arranging contrast-enhanced CT thorax to identify bleeding vessel. h) As per local policy, contacting either thoracic surgical colleagues or interventional radiology colleagues. i) Moving the patient to a high-care area with continuous monitoring.
Complications during post procedure lung expansion	Rapid lung expansion following insertion of the chest drain post LAT can lead to severe pain, coughing, and/or vasovagal syncope. Although such symptoms usually settle rapidly once complete expansion is achieved, they may require the chest tube to be opened to atmosphere to allow the lung to partially collapse once more, particularly if the patient has a degree of non-expandable lung. It is strongly advised that the chest drain be sutured and secured prior to connecting to the drainage circuit, to avoid symptoms while interventions are still taking place.

CXR, chest X-ray; LAT, local anaesthetic thoracoscopy; US, ultrasound; VATS, video-assisted thoracic surgery

Appendix references

1. Cavanna L, Mordenti P, Berte R et al. Ultrasound guidance reduces pneumothorax rate and improves safety of thoracentesis in malignant pleural effusion: report on 445 consecutive patients with advanced cancer. *World J Surg Oncol* 2014;12:139.
2. Perazzo A, Gatto P, Barlascini C et al. Can ultrasound guidance reduce the risk of pneumothorax following thoracentesis? *J Bras Pneumol* 2014;40:6-12.
3. Ault MJ, Rosen BT, Scher J et al. Thoracentesis outcomes: a 12-year experience. *Thorax* 2015;70:127-32.
4. Cho HY, Ko BS, Choi HJ et al. Incidence and risk factors of iatrogenic pneumothorax after thoracentesis in emergency department settings. *Journal of thoracic disease* 2017;9:3728-34.
5. Shechtman L, Shrem M, Kleinbaum Y et al. Incidence and risk factors of pneumothorax following pre-procedural ultrasound-guided thoracentesis. *Journal of thoracic disease* 2020;12:942-8.
6. Touray S, Sood RN, Holdorf J et al. Incidence of iatrogenic complications following thoracentesis in an academic medical center. *Am J Respir Crit Care Med* 2017;195:A3561.
7. Hooper CE, Welham SA, Maskell NA, British Thoracic Society. Pleural procedures and patient safety: a national BTS audit of practice. *Thorax* 2015;70:189-91.
8. Perl S, Bondarenco M, Natif N et al. Thoracentesis under clopidogrel is not associated with excessive bleeding events: a cohort study. *Respir Res* 2020;21:281.
9. Senitko M, Ray AS, Murphy TE et al. Safety and tolerability of vacuum versus manual drainage during thoracentesis: a randomized trial. *J Bronchology Interv Pulmonol* 2019;26:166-71.
10. Vilkki VA, Gunn JM. Complications related to tube thoracostomy in Southwest Finland hospital district between 2004 and 2014. *Scand J Surg* 2020;109:314-9.
11. Kong VY, Oosthuizen GV, Sartorius B et al. An audit of the complications of intercostal chest drain insertion in a high volume trauma service in South Africa. *Ann R Coll Surg Engl* 2014;96:609-13.
12. Maritz D, Wallis L, Hardcastle T. Complications of tube thoracostomy for chest trauma. *S Afr Med J* 2009;99:114-7.
13. Jackson K, Kafi O, Bhullar DS et al. Complications after thoracocentesis and chest drain insertion: a single centre study from the North East of England. *Journal of Respiration* 2021;1:135-40.
14. Asciak R, Hallifax RJ, Mercer RM et al. The hospital and patient burden of indwelling pleural catheters: a retrospective case series of 210 indwelling pleural catheter insertions. *Respiration* 2019;97:70-7.
15. Tremblay A, Michaud G. Single-center experience with 250 tunnelled pleural catheter insertions for malignant pleural effusion. Chest 2006;129:362-8.
16. Fysh ETH, Tremblay A, Feller-Kopman D et al. Clinical outcomes of indwelling pleural catheter-related pleural infections: an international multicenter study. *Chest* 2013;144:1597-602.
17. Feller-Kopman DJ, Reddy CB, DeCamp MM et al. Management of malignant pleural effusions. An official ATS/STS/STR clinical practice guideline. *Am J Respir Crit Care Med* 2018;198:839-49.
18. Asciak R, Mercer RM, Hallifax RJ et al. Does attempting talc pleurodesis affect subsequent indwelling pleural catheter (IPC)-related non-draining septated pleural effusion and IPC-related spontaneous pleurodesis? *European respiratory journal open research* 2019;5:00208-2018.
19. Thomas R, Piccolo F, Miller D et al. Intrapleural fibrinolysis for the treatment of indwelling pleural catheter-related symptomatic loculations: a multicenter observational study. *Chest* 2015;148:746-51.
20. Van Meter ME, McKee KY, Kohlwes RJ. Efficacy and safety of tunneled pleural catheters in adults with malignant pleural effusions: a systematic review. *J Gen Intern Med* 2011;26:70-6.
21. Murthy SC, Okereke I, Mason DP et al. A simple solution for complicated pleural effusions. *J Thorac Oncol* 2006;1:697-700.
22. Vial MR, Ost DE, Eapen GA et al. Intrapleural fibrinolytic therapy in patients with nondraining indwelling pleural catheters. *J Bronchology Interv Pulmonol* 2016;23:98-105.
23. Wilshire CL, Louie BE, Aye RW et al. Safety and efficacy of fibrinolytic therapy in restoring function of an obstructed tunneled pleural catheter. *Ann Am Thorac Soc* 2015;12:1317-22.
24. de Fonseka D, Bhatnagar R, Maskell NA. Local anaesthetic (medical) thoracoscopy services in the UK. *Respiration* 2018;96:560-3.