Real-Time Ultrasound Elastography in the diagnosis of thyroid nodules: The ElaTION RCT

Supplementary material 1– tables

Table 1: Final recruitment per site

Hospital	NHS Trust	Recruitment
Lister Hospital	East and North Herts NHS Trust	224
Charing Cross Hospital	Imperial College Healthcare NHS Trust	210
Hammersmith Hospital		
St Mary's Hospital		
Kings College Hospital	King's College Hospital NHS Foundation Trust	88
Queen Alexandra Hospital	Portsmouth Hospitals NHS Trust	58
Leicester Royal Infirmary	University Hospitals of Leicester NHS Trust	60
Basildon University Hospital	Basildon and Thurrock University Hospitals NHS Foundation Trust	55
University Hospital of North Tees	North Tees and Hartlepool Hospitals NHS Foundation Trust	53
North Manchester General Hospital	Pennine Acute Hospitals NHS Trust	49
Northwick Park Hospital	London North West University Healthcare NHS Trust	41
St Mark's Hospital		
Ipswich Hospital	The Ipswich Hospitals NHS Trust	32
Queen Elizabeth Hospital Birmingham	University Hospitals of Birmingham NHS Foundation Trust	24
Southend University Hospital	Southend University Hospital NHS Foundation Trust	23
Luton & Dunstable University Hospital	Luton & Dunstable University Hospitals NHS Foundation Trust	16
Royal Berkshire Hospital	Royal Berkshire NHS Foundation Trust	18
Norfolk & Norwich University Hospital	Norfolk & Norwich University Hospitals NHS Foundation Trust	14
James Paget Hospital	James Paget University Hospitals NHS Foundation Trust	10
Ashford Hospital	Ashford and St Peter's Hospitals NHS Foundation Trust	4
St Peter's Hospital		
Castle Hill Hospital	Hull and East Yorkshire Hospitals NHS Trust	3

Table 2: FNAC assessment & result form return rate

		Expected[1]	Returned Complete[2]	Returned Incomplete	All Returned	Not Returned
1st FNAC	Assessment	978	977 (99.9%)	0 (0%)	977 (99.9%)	1 (0.1%)
	Result	977	975 (99.8%)	1 (0.1%)	976 (99.9%)	1 (0.1%)
2nd FNAC[3]	Assessment	705	524 (74%)	0 (0%)	524 (74%)	181 (26%)
	Result	524	491 (94%)	2 (0.4%)	493 (94%)	31 (6%)
3rd FNAC[3]	Assessment	272	86 (32%)	0 (0%)	86 (32%)	186 (68%)
	Result	86	80 (93%)	1 (1%)	81 (94%)	5 (6%)
4th FNAC[4]	Assessment	15	15 (100%)	0 (0%)	15 (100%)	0 (0%)
	Result	15	13 (87%)	0 (0%)	13 (87%)	2 (13%)
5th FNAC[4]	Assessment	1	1 (100%)	0 (0%)	1 (100%)	0 (0%)
	Result	1	1 (100%)	0 (0%)	1 (100%)	0 (0%)

[1]*Number of expected forms plus forms received that were not expected*

[2]*Complete with the information required for primary and secondary outcome measures*

[3]Another FNAC is expected if a final definitive diagnosis has not been reached and surgery is not expected

[4]Forms beyond the 3rd FNAC are not expected

Table 3: HADS form return rate

				Returned		
		Expected	Complete*	Incomplete	Total	Not Returned
HADS	Baseline prior to FNAC	982	938 (96%)	27 (3%)	965 (98%)	17 (2%)
	3 Months	966	633 (66%)	11 (1%)	644 (67%)	322 (33%)
	6 Months	961	601 (63%)	10 (1%)	611 (64%)	350 (36%)
	12 Months	951	561 (59%)	17 (2%)	578 (61%)	373 (39%)
EQ-5D	Baseline prior to baseline FNAC	982	942 (96%)	20 (2%)	962 (98%)	20 (2%)
	After Surgery	379	219 (58%)	2 (1%)	221 (58%)	158 (42%)
	3 Months	967	623 (64%)	19 (2%)	642 (66%)	325 (34%)
	6 Months	963	602 (63%)	7 (1%)	609 (64%)	354 (37%)
	12 Months	954	557 (58%)	17 (2%)	574 (60%)	380 (40%)

*Both sub-scales complete (note a subscale is permitted at most one missing item for score calculation)

Table 4: Surgery forms return rates

	Expected	Returned Complete	Returned Incomplete	All Returned	Not Returned
Surgical Decision	246*	220 (89%)**	26 (11%)	246 (100%)	0 (0%)
Histology	380$^\alpha$	379 (99.7%)	0 (0%)	379 (99.7%)	1 (0.3%)
30 Day Post-Operative	380$^\alpha$	377 (99%)	0 (0%)	377 (99%)	3 (1%)
6 Month Post-Operative	380$^\alpha$	373 (98%)	0 (0%)	373 (98%)	7 (2%)

*all forms returned 'expected'

**completed if date surgery planned is filled in

α includes one participant who returned form with date of surgery but we have no histology form for

Table 5: Number of Thy 1 results following first FNAC by trial arm – excluding cytologist centres

	USE-FNAC	US-FNAC	Adjusted* Risk Difference (95% C.I)	Risk Difference (95% C.I)	p-value**
Primary Outcome	N=444	N=443			
N(%)	76 (17%)	64 (14%)	0.032 (-0.006 to 0.069)	0.027 (-0.021 to 0.075)	0.10

A negative difference favours the USE-FNAC arm.

*Adjusting for minimisation variables

Table 6: Number of Thy 1 results following first FNAC by trial arm - including only radiologists

	USE-FNAC	US-FNAC	Adjusted* Risk Difference (95% C.I)	Risk Difference (95% C.I)	p-value**
Primary Outcome	N=461	N=456			
N(%)	78 (17%)	73 (16%)	0.015 (-0.020 to 0.050)	0.009 (-0.039 to 0.057)	0.41

positive about elastography

A negative difference favours the USE-FNAC arm.

*Adjusting for minimisation variables

**p-value taken from adjusted model

Table 7: Number of thyroidectomies

	USE-FNAC	US-FNAC	Adjusted* Risk Difference (95% C.I)	Risk Difference (95% C.I)	p-value**
	N=493	N=489			
N(%)	183 (37%)	196 (40%)	-0.02 (-0.06 to 0.009)	-0.03 (-0.09 to 0.03)	0.15

A negative difference favours the USE-FNAC arm.

*Adjusting for minimisation variables

**p-value taken from adjusted model

Table 8: Final Definitive Diagnosis (FDD) category by test arm

		USE-FNAC	US-FNAC	Total
Number randomised		493	489	982

		N=346	N=342	N=688
FDD Classification	Histology Result	168 (49%)	180 (53%)	348 (51%)
	2 Thy2s & US 2 and Thy 2	71 (21%)	66 (19%)	137 (20%)
	US 2 and Thy 2	46 (13%)	45 (13%)	91 (13%)
	2 Thy 2s	46 (13%)	35 (10%)	81 (12%)
	US 2 & Histology Result	11 (3%)	12 (4%)	23 (3%)
	All FDD Criteria	4 (1%)	2 (1%)	6 (2%)
	2 Thy 2s & Histology Result	0 (0%)	2 (1%)	2 (0.3%)

		2nd FNAC Result							
		No result	Thy 1	Thy 2	Thy 3a	Thy 3	Thy 4	Thy 5	**Total**
1st FNAC Result	No result	7* (2%)	0 (0%)	0(0%)	0 (0%)	0(0%)			7 (2%)
	Thy 1	20 (7%)	29 (10%)	18 (6%)	8 (3%)	2 (1%)			77 (26%)
	Thy 2	76 (26%)	11 (4%)	-	13 (4%)	2 (1%)			102 (35%)
	Thy 3a	20 (7%)	7 (2%)	19 (6%)	33 (11%)	2 (1%)			81 (28%)
	Thy 3	16 (11%)	2 (1%)	0 (%)	0 (0%)	1 (0.3%)			19 (6%)
	Thy 4	2 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)			2 (1%)
	Thy 5	6 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)			6 (2%)
	Total	147 (50%)	49 (17%)	37 (13%)	54 (18%)	7 (2%)			**294**

Table 9: FNAC Results for Participants without a Final Definitive Diagnosis

*4 participants withdrawn; 1 participant's nodule disappeared; 1 1st FNAC result not returned; and 1 participant's 1st FNAC returned incomplete

Table 10: Number of FNACs until Final Definitive Diagnosis

		USE-FNAC	US-FNAC	Adjusted* Odds Ratio (96% CI)	Odds Ratio (95% CI)	p-value
Number of FNACs:		N=346	N=342			
	1 FNAC	168 (49%)	175 (51%)	1.10 (0.82 to 1.49)	1.11 (0.83 to 1.48)	0.53
	2 FNACs	151 (44%)	142 (42%)			
	3 FNACs	22 (6%)	21 (6%)			
	4 FNACs	4 (1%)	4 (1%)			
	5 FNACS	1 (0.3%)	0 (0%)			
Median (IQR)		2.0 (1.0-2.0)	1.0 (1.0-2.0)			

A ratio less than 1 favours the USE-FNAC arm.

*Adjusting for minimisation variables

**p-value taken from adjusted model

Table 11: Mean HADS subscale scores over follow up by test arm

	USE-FNAC	US-FNAC	**Mean Difference*** **(95% C.I.)**	**p-value**
	N=493	N=484		
Anxiety Subscale				
	N=470	N=474		
Baseline Prior to Any FNAC	6.93 (4.41)	6.44 (4.30)	-	-
	N=337	N=298		
3 Months After 1 FNAC Result	6.57 (4.84)	6.46 (4.54)	0.11 (-0.62 to 0.85)	0.77

	N=312	N=291		
6 Months After 1st FNAC Result	6.37 (4.66)	6.49 (4.99)	-0.12 (-0.89 to 0.65)	0.76
	N=295	N=267		
12 Months After 1st FNAC Result	6.12 (4.74)	6.12 (4.74)	-0.002 (-0.79 to 0.78)	1.00
Depression Subscale				
	N=470	N=470		
Baseline Prior to Any FNAC	3.76 (3.59)	3.45 (3.54)	-	-
	N=335	N=299		
3 Months After 1 FNAC Result	4.36 (4.22)	4.05 (4.23)	0.31 (-0.35 to 0.97)	0.36
	N=315	N=289		
6 Months After 1st FNAC Result	4.10 (4.15)	4.38 (4.49)	-0.28 (-0.97 to 0.41)	0.43
	N=295	N=268		
12 Months After 1st FNAC Result	3.96 (4.31)	3.93 (4.31)	0.02 (-0.69 to 0.74)	0.95

Estimates are presented as Means (SD) unless otherwise specified.
A negative difference favours the USE-FNAC arm
*Using two-sample t-test

Table 12: Repeated measures analysis for HADS depression subscale score

	Adjusted Mean Difference* (95% C.I.)	Mean Difference (95% C.I.)	p-value**
Intercept	0.53 (0.22 to 0.84)	0.61 (0.39 to 0.83)	0.0009
Depression Baseline Subscale Score	0.91 (0.87 to 0.94)	0.91 (0.87 to 0.94)	<0.0001
USE-FNAC vs US-FNAC	-0.006 (-0.27 to 0.26)	-0.005 (-0.27 to 0.26)	0.97
HADS Assessment No.	0.07 (0.04 to 0.09)	0.07 (0.04 to 0.09)	<0.0001
HADS Assessment No*Test	-0.04 (-0.07 to -0.003)	-0.04 (-0.07 to -0.003)	0.03
Intercept	0.60 (0.30 to 0.91)	0.68 (0.47 to 0.89)	0.0001
Depression Baseline Subscale Score	0.91 (0.87 to 0.94)	0.91 (0.87 to 0.94)	<0.0001
USE-FNAC vs US-FNAC	-0.15 (-0.38 to 0.09)	-0.14 (-0.38 to 0.09)	0.23
HADS Assessment No.	0.05 (0.03 to 0.07)	0.05 (0.03 to 0.07)	<0.0001

A negative difference favours the USE-FNAC arm
*Adjusting for minimisation variables
** p-value taken from adjusted model

Table 13: Mean EQ5D 3L scores over follow up by test arm

	USE-FNAC	US-FNAC	Mean Difference* (95% C.I.)	p-value
	N=493	N=484		
	N=468	N=474		
Baseline	0.81 (0.20)	0.81 (0.20)	-	-

	N=107	N=114		
After Surgery	0.71 (0.20)	0.75 (0.15)	0.04 (-0.005 to 0.09)	0.08
	N=330	N=293		
3 Months After Randomisation	0.78 (0.23)	0.80 (0.21)	0.03 (-0.005 to 0.06)	0.10
	N=312	N=290		
6 Months After Randomisation	0.80 (0.20)	0.79 (0.21)	-0.007 (-0.04 to 0.03)	0.69
	N=293	N=264		
12 Months After Randomisation	0.80 (0.21)	0.81 (0.21)	0.01 (-0.02 to 0.05)	0.56

A negative difference favours the USE-FNAC arm
Estimates are presented as Means (SD) unless otherwise specified.
*Using two-sample t-test

Table 14: Repeated measures analysis for EQ5D 3L score

	Adjusted Mean Difference* (95% C.I.)	Mean Difference (95% C.I.)	p-value**
Intercept	0.11 (0.08 to 0.14)	0.10 (0.07 to 0.13)	<0.0001
Baseline EQ5D Score	0.87(0.84 to 0.90)	0.87 (0.84 to 0.90)	<0.0001
SE-FNAC vs US-FNAC	0.002 (-0.01 to 0.02)	0.002 (-0.01 to 0.02)	0.81
EQ5D Assessment No.	-0.001 (-0.003 to 0.001)	-0.001 (-0.003 to 0.001)	0.19
EQ5D Assessment No*Test	0.0004 (-0.002 to 0.003)	0.0004 (-0.002 to 0.003)	0.73
Intercept	0.11 (0.08 to 0.14)	0.10 (0.07 to 0.13)	<0.0001
Baseline EQ5D Score	0.87 (0.84 to 0.90)	0.87 (0.84 to 0.90)	<0.0001
SE-FNAC vs US-FNAC	0.004 (-0.009 to 0.02)	0.003 (-0.009 to 0.02)	0.56
EQ5D Assessment No.	-0.001 (-0.002 to -0.0002)	-0.001 (-0.002 to -0.0002)	0.02

A negative difference favours the USE-FNAC arm
*Adjusting for minimisation variables
**p-value taken from adjusted model

Table 15: Sensitivity analyses of 1st FNAC compared with 2nd FNAC accuracy in malignant nodules

	2nd FNAC Malignant	2nd FNAC Benign	Total	1st FNAC Sensitivity	2nd FNAC Sensitivity
Assuming Thy 1 results are benign					
1st FNAC Malignant	7	0	7	0.35 (0.15, 0.59)	0.80 (0.56, 0.94)
1st FNAC Benign	9	4	13		
Total	16	4	20	p=0.003	
Assumptions placed on missing FDD					
1st FNAC Malignant	43	19	62	0.75 (0.64, 0.84)	0.77 (0.67, 0.86)
1st FNAC Benign	21	0	21		
Total	64	19	83	p=0.75	
Assuming Thy 1 results are benign and assumptions placed on missing FDD					
1st FNAC Malignant	43	28	71	0.62 (0.53, 0.71)	0.68 (0.59, 0.76)
1st FNAC Benign	34	9	43		
Total	77	37	114	p=0.45	

Table 16: Sensitivity analyses of 1st FNAC compared with 2nd FNAC accuracy in benign nodules

	2nd FNAC Malignant	2nd FNAC Benign	Total	1st FNAC Specificity	2nd FNAC Specificity
Assuming Thy 1 results are malignant					
1st FNAC Malignant	45	37	82	0.75 (0.70, 0.79)	0.73 (0.68, 0.77)
1st FNAC Benign	44	198	242		
Total	89	235	324	p=0.44	
Assumptions placed on missing FDD*					
1st FNAC Malignant	17	10	27	0.89 (0.85, 0.93)	0.84 (0.80, 0.89)
1st FNAC Benign	22	198	220		
Total	39	208	247	p=0.03	
Assuming Thy 1 results are malignant and assumptions placed on missing FDD					
1st FNAC Malignant	46	55	101	0.71 (0.67, 0.76)	0.72 (0.67, 0.76)
1st FNAC Benign	54	198	252		
Total	100	253	353	p=0.92	

*Note that we have the same numbers as for the primary analysis. This is due to the fact those with a missing FDD, who have one Thy 2 result, and potentially other Thy 1 results, have been assumed to be 'Benign'. However, to compare 1st with 2nd FNAC results, we need both a 1st and 2nd diagnostic result for the participant) (i.e. not a Thy 1 result). So when excluding participants who do not have a diagnostic 1st and 2nd FNAC result, we are also excluding those who assumptions have been made for.

Table 17: Sensitivity analyses of agreement between 1st FNAC and 2nd FNAC

	2nd FNAC Malignant	2nd FNAC Benign	Total
Assuming Thy 1 results are benign			
1st FNAC Malignant	60	42	102
1st FNAC Benign	67	322	389
Total	127	364	491
Assuming Thy 1 results are malignant			
1st FNAC Malignant	143	74	217
1st FNAC Benign	76	198	274
Total	219	272	491

Table 18: Sensitivity analyses of US-alone compared with US-FNAC accuracy in malignant nodules

	US-FNAC Malignant	US-FNAC Benign	Total	US-alone Sensitivity	US-FNAC Sensitivity
Assuming Thy 1 results are benign					
US-alone Malignant	63	9	72	0.91 (0.85, 0.97)	0.85 (0.77, 0.93)
US-alone Benign	4	3	7		
Total	67	12	79	p=0.17	
Assumptions placed on missing FDD					
US-alone	114	15	129	0.90	0.87

				(0.85, 0.95)	(0.82, 0.93)
Malignant					
US-alone Benign	11	3	14		
Total	125	18	143	p=0.43	
Assuming Thy 1 results are benign and assumptions placed on missing FDD					
US-alone Malignant	114	24	138	0.90 (0.85, 0.95)	0.82 (0.76, 0.88)
US-alone Benign	11	4	15		
Total	125	28	153	p=0.03	

Table 19: Sensitivity analyses of US-USE alone compared with USE-FNAC accuracy in malignant nodules

	USE-FNAC Malignant	USE-FNAC Benign	Total	USE-US Sensitivity	USE-FNAC Sensitivity
Assuming Thy 1 results are benign					
USE-US Malignant	45	8	53	0.76	0.84
USE-US Benign	14	3	17	(0.66, 0.86)	(0.76, 0.93)
Total	59	11	70	p=0.20	
Assumptions placed on missing FDD					
USE-US Malignant	67	4	71	0.58	0.89
USE-US Benign	42	9	51	(0.49, 0.67)	(0.84, 0.95)
Total	109	13	122	p<0.0001	
Assuming Thy 1 results are benign and assumptions placed on missing FDD					
USE-US Malignant	67	11	78	0.58	0.81
USE-US Benign	42	14	56	(0.50, 0.67)	(0.75, 0.88)
Total	109	25	134	p<0.0001	

Table 20: Sensitivity analyses of US-alone compared with US-FNAC accuracy in benign nodules

	US-FNAC Malignant	US-FNAC Benign	Total	US-FNAC Specificity	US-FNAC Specificity
Assuming Thy 1 results are malignant					
US-alone Malignant	80	61	141	0.46 (0.40, 0.52)	0.60 (0.54, 0.66)
US-alone Benign	25	97	122		
Total	105	158	263	p=0.0001	
Assumptions placed on missing FDD					
US-alone Malignant	61	103	164	0.41 (0.35, 0.47)	0.72 (0.67, 0.77)
US-alone Benign	16	97	113		
Total	77	200	277	p<0.0001	
Assuming Thy 1 results are malignant and assumptions placed on missing FDD					
US-alone Malignant	90	103	193	0.39 (0.33, 0.44)	0.63 (0.58, 0.69)
US-alone Benign	25	97	122		
Total	115	200	315	p<0.0001	
Excluding U3					
US-alone Malignant	5	8	13	0.90 (0.84,	0.83 (0.77,

US-alone Benign	16	97	113	0.95)	0.90)
Total	21	105	126	p=0.1	
Excluding U3 & Thy 3a					
US-alone Malignant	1	8	9	0.92 (0.87,	0.91 (0.86,
US-alone Benign	9	97	106	0.97)	0.96)
Total	10	105	115	p=0.8	
Excluding U3/Th3, Thy3f, Thy 3a					
US-alone Malignant	1	8	9	0.92 (0.86,	0.99 (0.95,
US-alone Benign	0	97	97	0.97)	1.00)
Total	1	105	106	p=0.05	

Table 21: Sensitivity analyses of US-USE alone compared with USE-FNAC accuracy in benign nodules

	USE-FNAC Malignant	USE-FNAC Benign	Total	USE-US Specificity	USE-FNAC Specificity
Assuming Thy 1 results are malignant					
USE-US Malignant	51	65	116	0.58 (0.52, 0.64)	0.65 (0.60, 0.71)
USE-US Benign	45	115	160		
Total	96	180	276	p=0.06	
Assumptions placed on missing FDD					
USE-US Malignant	34	85	119	0.59 (0.53, 0.65)	0.77 (0.72, 0.82)
USE-US Benign	32	139	171		
Total	66	222	290	p<0.0001	
Assuming Thy 1 results are malignant and assumptions placed on missing FDD					
USE-US Malignant	34	107	141	0.57 (0.52, 0.62)	0.80 (0.76, 0.84)
USE-US Benign	32	156	188		
Total	66	263	329	p<0.0001	

Table 22: Radiologists' feedback from any FNAC

		USE-Arm
		N=815
Was the nodule suitable to be biopsied in your view?	Yes	756 (93%)
	No	34 (4%)
	missing	25 (3%)
If no, please select why:		
	Pure cystic lesion	1 (3%)
	No normal tissue surrounding it	12 (33%)
	Pathology separate to thyroid	5 (14%)
	Benign nodule	5 (14%)

	Other	17 (47%)
	missing	1 (3%)
Did the elastography technique help you in identifying the nodule required for FNAC	Yes	105 (13%)
	No	663 (81%)
	N/A	8 (1%)
	missing	39 (5%)
Did the elastography technique help you identify the specific part within the nodule for FNAC?	Yes	174 (21%)
	No	608 (75%)
	N/A	4 (0.5%)
	missing	29 (4%)
Did you find the real time elastography to be helpful over and above the conventional ultrasound in determining malignancy?	Yes	264 (32%)
	No	525 (64%)
	N/A	1 (0.1%)
	missing	25 (3%)

Table 23: Description of Complication Rates by Category

	Complication details
Bleeding requiring return to theatre	Post thyroidectomy bleeding/neck haematoma requiring return to theaters on . Procedures included inc./drain haematomastion, exploration thyroid, haemostasis post op and irrigation of wound. Evacuation of haemotoa
	1 details not given
Haematoma not requiring evacuation	seroma noted underneath the skin flap-drained
Wound infection	attended walk-in . Given antibiotics for WI centre
	Infection post total to wound flucloxacillin prescribed
	flucloxacillin 7/7
	5 details not given
Hypocalcaemia requiring replacement	calcium under 1.84(adjusted), asymptomatic, oral calcium given increased te 2.09
	Corrected calcium 1.96, given calcium supplement. resolved at follow-up
	Hypocalcaemia requiring replacement calcium? mild episodes solved with sandacl at clinic review
	Hypocalcaemia requiring replacement calcium? whilst in hospital
	11 details not given
Vocal cord palsy*	SAE and . Both vocal cords mobile dated & equal
	1 details not given
Keloid scarring*	Quite lumpy SAD
	Keloid scarring? MILD
	1 details not given
Death	Multiple organ failure due to cancer
	Bowel obstruction

Table 24: SAEs Numbers by Test

	USE-FNAC	US-FNAC

	N=493	N=489
Number of SAEs	10	4
Number of patients with an SAE	9 (2%)	4 (1%)

Table 25: SAE description by test

Pat_TNO	Randomisation Date	Event Start Date	Event Description	Event Ceased Date	Causality
USE-FNAC					
1082	02/11/2015	15/12/2015	Died – multiple organ failure due to cancer	03/01/2016	Probably not related to trial
1083	09/11/2015	05/02/2017	Died – collapse and cardiac arrest at home following left VATS lobectomy	06/02/2017	Probably not related to trial
1168	07/04/2016	14/062016	Disability – reviewed by ENT consultant	24/01/2018	Probably not related to trial
1301	19/08/2016	16/09/2016	Required Hospitalisation for 9 days - cardiac/anticoag appointments made	Ongoing	Probably not related to trial
1364	24/10/2016	25/02/2016	Required Hospitalisation following surgery so expected	27/02/2017	Probably not related to trial
1504	23/03/2017	16/05/2017	Required hospitalisation for 10 days following intracranial surgery	26/05/2017	Probably not related to trial
1736	24/10/2017	30/11/2017	Bladder carcinoma diagnosis	23/01/2018	Probably not related to trial
1826	30/01/2018	01/03/2018	Required hospitalisation for 3 days – re-operation due to surgical complications	03/03/2018	Probably not related to trial
1826	30/01/2018	11/03/2018	Required hospitalisation for 29 days - Patient well, afebrile, would almost completely healed. Discharged 08Apr18 - Patient will require long term IV therapy (IV teicoplanon 1.2g OD) for MRSA bacteraemia.	08/04/2018	Not related to the trial – confirmed via email 08/08/2018
1934	01/06/2018	19/10/2018	Died - metastatic uterine leiomyosarcoma	27/10/2018	Probably not related to the trial
US-FNAC					
1655	14/08/2017	16/09/2017	Required hospitalisation for 6 days – following thyroidectomy. Bloods confirmed hypocalcaemia resulting in prolonged admission	21/09/2018	Probably not related to the trial
1829	01/02/2018	04/08/2018	Died – admitted due to bowel obstruction and passed away	18/08/2018	Probably not related to the trial

1893	23/04/2018	06/07/2018	Died – cerebral metastatic melanoma	07/07/2018	Probably not related to the trial
1965	23/07/2018	15/03/2019	Died – acute tracheal obstruction	04/04/2018	Probably not related to the trial