

CHAPTER 4

Paediatric Renal Biopsies

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4.1: Introduction

This chapter reports on renal biopsies done in children less than 15 years of age in Malaysia. Data on native kidney biopsies were collected from 1999 in Department of Paediatrics Hospital Kuala Lumpur. With the establishment of the Malaysian Renal Biopsy Registry (MRRB) in 2005, other Ministry of Health (MOH) Hospitals started submitting data on renal biopsies performed. This chapter includes data from 1999 to 2007 for Hospital Kuala Lumpur and from 2005 to 2007 for other MOH Hospitals.

4.2: Number of patients and renal biopsies

4.2.1: Total number of patients and native renal biopsies

The Registry recorded the diagnosis and clinical data of 640 renal biopsies in 579 children.

4.2.2: Number of native renal biopsies from various hospitals
Hospital Kuala Lumpur reported an average of 35 native biopsies per year. The other MOH Hospitals collected data for 287 renal biopsies (Table 4.2.2).

Table 4.2.2: Number of renal biopsies

Year	Hospital Kuala Lumpur	Other MOH Hospitals
1999	37	-
2000	29	-
2001	28	-
2002	29	-
2003	53	-
2004	36	1*
2005	40	83
2006	37	91
2007	30	112
Total	319	287

* 1 submission from other MOH Hospital prior to MRRB

4.3: Outcome of renal biopsies

Altogether 606(94.7%) renal biopsies were assessed to be adequate for diagnosis upon review by nephrologists and histopathologists. A total of 34(5.3%) biopsies were not conclusive. Thailand, United Kingdom and Japan reported success rates of between 93.4% and 98.7%.^(1,2,3) Thus the success rate in the present report is comparable with figures reported by other centers.

4.4: Patient characteristics

Table 4.4 shows that renal biopsies were performed on 275 (47.5%) boys and 304 (52.5%) girls. The higher number in girls was probably attributed to biopsies among children with systemic lupus erythematosus. The mean age at biopsy was 9.3 ± 3.9 years. The racial distribution of the patients was Malay 64%, Chinese 19%, Indian 7.3% and other ethnic groups 9.7%.

Table 4.4: Gender and racial distribution

		No	%
Gender	Male	275	47.5
	Female	304	52.5
	Total	579	100
Race	Malay	371	64.0
	Chinese	110	19.0
	Indian	42	7.3
	Others	56	9.7
	Total	579	100

4.5: Clinical presentation

4.5.1: Clinical presentation at biopsy

Nephrotic syndrome was the most frequent clinical presentation accounting for 55.9%. The second commonest indication for performing renal biopsy was nephritic syndrome, which contributed to 14.0% of cases (Table 4.5.1).

Singapore, Hong Kong and Thailand reported nephrotic syndrome as their commonest clinical presentation at biopsy in 67%, 69% and 42.3% respectively. ^(1,4,5)

4.5.2: Renal function at biopsy

Twenty nine percent of biopsies were performed in the setting of impaired renal function (Table 4.5.2).

4.6: Diagnosis of paediatric renal biopsies

Of 606 with final diagnosis following renal biopsy, focal segmental glomerulosclerosis (FSGS) contributed the largest group at 27.2%. It is hence not surprising that FSGS is the commonest cause of childhood end stage renal disease secondary to glomerular disease in Malaysia. The other common glomerulonephritis (GN) was lupus nephritis (26.1%). Minimal change disease (MCD) was diagnosed in 17.8% of cases and post-infectious glomerulonephritis (GN) in 10.0%. IgA nephropathy accounted for 4.4% and Henoch Schonlein Purpura 2.6% (Table 4.6). In comparison, IgA nephropathy was the most common glomerulonephritis in Italy.⁽⁶⁾ This is most probably due to differences in biopsy practices.

Table 4.5.1: Clinical presentation at biopsy

Clinical presentation	Number	%
Asymptomatic urine abnormalities	67	11.1
Nephritic syndrome	85	14.0
Nephrotic syndrome	339	55.9
Nephritic nephrotic syndrome	46	7.6
Unknown	69	11.4
Total	606	100

Table 4.5.2: Renal function at biopsy

Renal function at biopsy	Number	%
Impaired	177	29.2
Normal	386	63.7
Unknown	43	7.1
Total	606	100

Table 4.6: Diagnosis of paediatric renal biopsies

Diagnosis	Number	%
FSGS	165	27.2
Lupus nephritis	158	26.1
MCD	108	17.8
Post-infectious GN	61	10.0
IgA nephropathy	27	4.4
Henoch Schonlein Purpura	16	2.6
Mesangial proliferative GN non-IgA	13	2.1
Advanced glomerulosclerosis	7	1.2
HUS/TTP	6	1.0
Membranoproliferative GN	6	1.0
Acute tubular necrosis	6	1.0
Vasculitis	3	0.5
Membranous nephropathy	3	0.5
Chronic interstitial nephritis	2	0.3
Acute interstitial nephritis	2	0.3
Alport's syndrome	2	0.3
Hereditary(others)	1	0.3
Malignancy	1	0.2
Crescentic GN	1	0.2
Idiopathic crescentic ANCA	1	0.2
Others	3	0.5
Unknown	14	2.3
Total	606	100

4.7: Renal histopathology diagnosis of children presenting with nephrotic syndrome

Nephrotic syndrome was the clinical diagnosis in 339 biopsies. The indications for renal biopsy were steroid resistant nephrotic, atypical nephrotic syndrome, or for assessment of cyclosporine nephrotoxicity in steroid responsive nephrotic syndrome. As shown in table 4.7, FSGS was found in 44.5% and MCD in 28.3%.

In Hong Kong, the most common histology finding for nephrotic syndrome was minimal change (59%) followed by FSGS which accounted for 9% of cases. The indications for biopsy in their center included nephrotic syndrome with frequent relapses, steroid dependence and atypical features.⁽⁵⁾ Minimal change disease was the most common underlying renal pathology in Korea.⁽⁶⁾ The Korean indications for biopsy in nephrotic syndrome were unusual clinical manifestations or steroid resistance. The different histological findings may be due to different practice pattern.

4.8: Renal histopathology diagnosis of children presenting with nephritic syndrome.

Renal biopsy was performed in 85 children with nephritic syndrome. The majority demonstrated post-infectious GN (44.7%), while the others had lupus nephritis (31.8%), Henoch Schonlein Purpura (5.9%) and IgA nephropathy (5.9%) (Table 4.8). In contrast, IgA nephropathy was the most frequent diagnosis of renal biopsies in children with nephritic syndrome in Italy.⁽⁷⁾

Table 4.7: Renal histopathology diagnosis of children presenting with nephrotic syndrome

Diagnosis	Number	%
FSGS	151	44.5
MCD	96	28.3
Lupus nephritis	55	16.2
IgA nephropathy	9	2.6
Mesangial proliferative GN non-IgA	8	2.4
Post-infectious GN	6	1.8
Others*	12	3.5
Unknown	2	0.7
Total	339	100.0

* (membranous nephropathy, membranoproliferative GN, crescentic GN, Henoch Schonlein Purpura, HUS/TTP, vasculitis, hereditary renal disease, acute interstitial nephritis, chronic interstitial nephritis, advance glomerulosclerosis)

Table 4.8: Renal histopathology diagnosis of children presenting with nephritic syndrome

Diagnosis	Number	%
Post-infectious GN	38	44.7
Lupus nephritis	27	31.8
Henoch Schonlein Purpura	5	5.9
IgA nephropathy	5	5.9
FSGS	3	3.5
Others*	5	5.9
Unknown	2	2.3
Total	85	100.0

* (membranoproliferative GN, mesangial proliferative GN-non IgA, Alport's syndrome, acute tubular necrosis)

4.9: Causes of acute renal failure

The causes of acute renal failure were post-infectious GN (29.8%), lupus nephritis (29.8%), FSGS (8.7%), and HUS/TTP (5.8%). In the registry, 5.8% of renal failure was due to advanced glomerulosclerosis (Table 4.9).

In Italy the three commonest causes of acute renal failure were crescentic glomerulonephritis, acute interstitial nephritis and hemolytic uremic syndrome, each accounting for 12%.⁽⁷⁾

Table 4.9: Causes of acute renal failure in children who underwent renal biopsy

Diagnosis	Number	%
Post-infectious GN	31	29.8
Lupus nephritis	31	29.8
FSGS	9	8.7
Advanced glomerulosclerosis	6	5.8
HUS/TTP	6	5.8
Acute tubular necrosis	4	3.8
MCD	3	2.9
Acute interstitial nephritis	2	1.9
IgA nephropathy	2	1.9
Others*	6	5.8
Unknown	4	3.8
Total	104	100.0

*(membranoproliferative GN, mesangial proliferative GN non-IgA, crescentic, Henoch schlein purpura, vasculitis, malignancy)

4.10: Paediatric focal segmental glomerulosclerosis and minimal change disease

4.10.1: Characteristics of paediatric focal segmental glomerulosclerosis and minimal change disease

There was no difference in term of age at presentation, gender and urine albumin excretion rate in children with FSGS or MCD. However, there was a significant difference in the racial composition between the two groups. The percentage of Indian children with FSGS was much higher compared to MCD. Children with FSGS had lower creatinine clearance at biopsy (Table 4.10.1).

Table 4.10.1: Characteristic of paediatric focal segmental glomerulosclerosis and minimal change disease

Clinical characteristics		FSGS	MCD	p Value
Number		165	108	
Mean age (year)		8.0 (SD=4.0)	8.5 (SD=4.3)	0.39
Median age (year)		8.3	9.0	
Race		N (%)	N (%)	0.04
	Malay	110 (66.7%)	69 (63.9%)	
	Indian	23 (13.9%)	6 (5.6%)	
	Chinese	19 (11.5%)	23 (21.3%)	
	Others	13 (7.9%)	10 (9.2%)	
	Total	165 (100%)	108 (100%)	
Gender		99/66 (1.5:1)	67/41 (1.6:1)	0.74
N		165	108	0.03
Creatinine Clearance (CrCl) ml/min/1.73m ²	CrCl <30	14 (8.5%)	5 (4.6%)	
	CrCl 30-60	22 (13.3%)	5 (4.6%)	
	CrCl 60-90	25 (15.2%)	14 (13.0%)	
	CrCl > 90	104 (63.0%)	84 (77.8%)	
24HUP g (N, mean)		N=35, 3.6	N=30, 2.5	0.17
Urine albumin mg /m ² /H (N, mean)		N=46, 182.8	N=26, 97.8	0.10
Albumin g/L (N, mean)		N=155, 24.08	N=100, 26.55	0.08

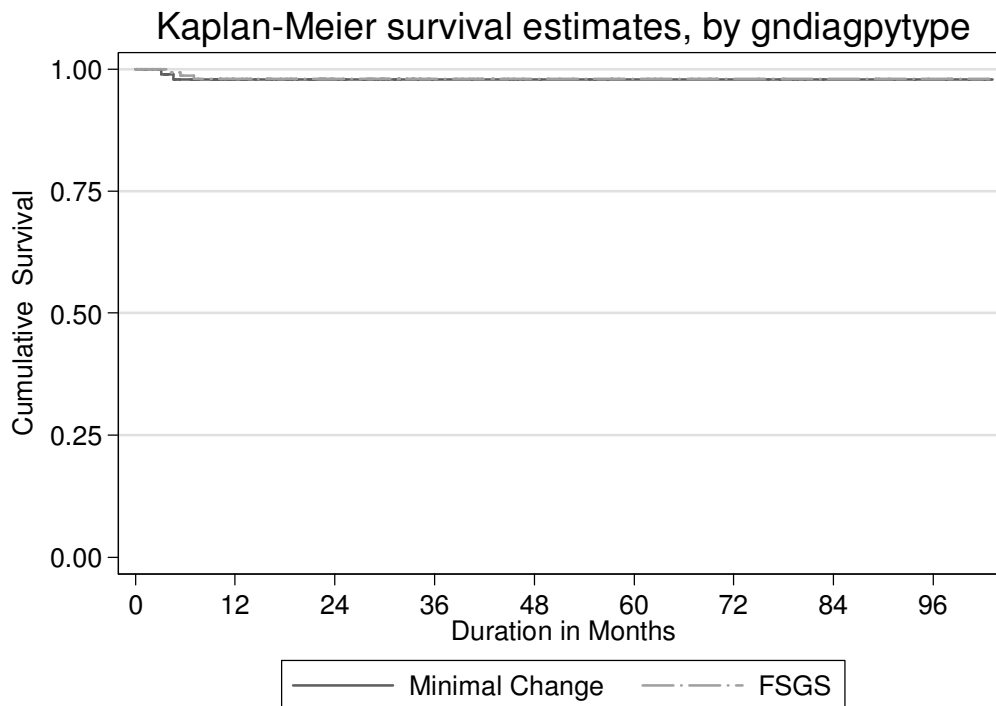
4.10.2: Patient survival in focal segmental glomerulosclerosis and minimal change disease

Table 4.10.2 and Figure 4.10.2 shows that patient survival was similar for both FSGS and MCD; 98% at 3 years and 5 years from the time of renal biopsy.

Table 4.10.2: Patient survival for focal segmental glomerulosclerosis and minimal change disease

Renal Histopathology diagnosis Interval (months)	Minimal change disease			FSGS		
	No	% survival	SE	No	% survival	SE
0	102	100	-	145	100	-
12	58	98	0	110	98	0
24	34	98	0	73	98	0
36	25	98	0	45	98	0
48	20	98	0	34	98	0
60	14	98	0	26	98	0
72	14	98	0	18	98	0
84	7	98	0	14	98	0
96	5	98	0	6	98	0

Figure 4.10.2: Kaplan Meier patient survival by focal segmental glomerulosclerosis and minimal change disease



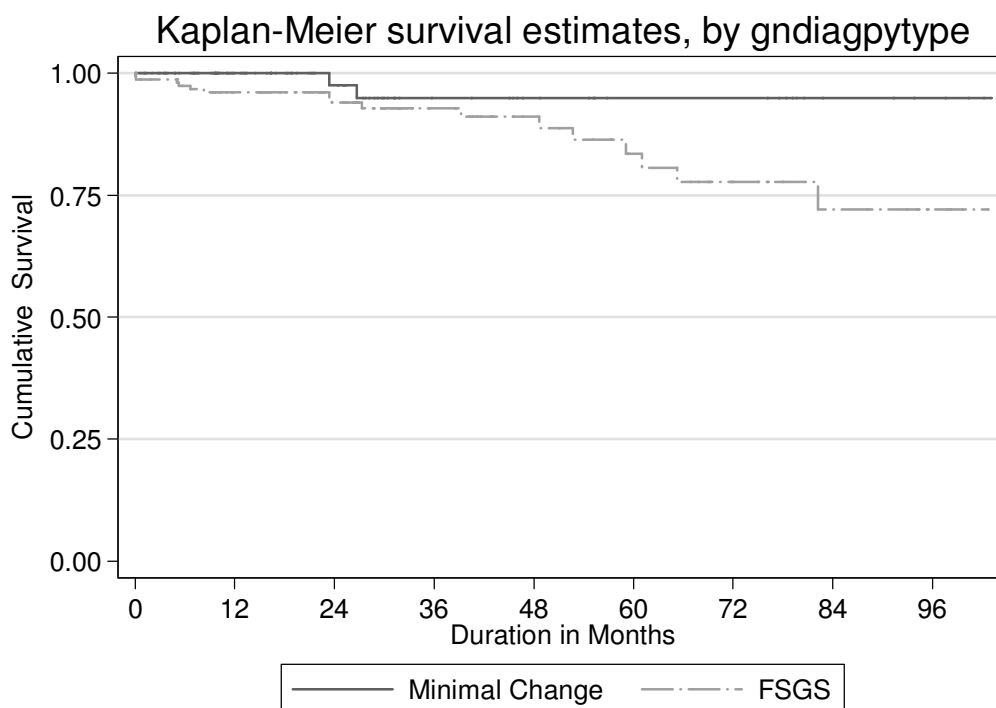
4.10.3: Renal survival of patient with focal segmental glomerulosclerosis and minimal change disease

The renal survival data was extracted from the Malaysia Dialysis Transplant Registry. Table 4.10.3 and Figure 4.10.3 show that FSGS has poorer renal survival; 92% and 82% at 3 years and 5 years respectively. Renal survival for MCD at 3 years and 5 years remained at 94%.

Table 4.10.3: Renal survival of patient with focal segmental glomerulosclerosis and minimal change disease

Renal Histopathology diagnosis Interval (days)	Minimal change disease			FSGS		
	No	% survival	SE	No	% survival	SE
0	92	100	-	142	100	0
12	52	100	-	111	96	0
24	33	97	0	80	93	0
36	25	94	0	52	92	0
48	20	94	0	40	90	0
60	14	94	0	29	82	0
72	14	94	0	19	76	0
84	7	94	0	14	71	0
96	5	94	0	6	71	0

Figure 4.10.3: Kaplan Meier renal survival by focal segmental glomerulosclerosis and minimal change



4.11: Paediatric lupus nephritis

There were 158 renal biopsies performed for 146 children with lupus.

4.11.1: Patient characteristics of paediatric lupus nephritis

The female: male ratio was 5.9:1 reflecting the preponderance of lupus in females. The racial distribution for paediatric lupus nephritis was Malay (63.7%), Chinese (26.7%), Indian (3.4%) and others (6.2%).

4.11.2: Extra renal manifestation of paediatric SLE

The most common extra renal manifestations among 130 children were cutaneous involvement (malar rash in 66.9%, photosensitivity in 39.2%, oral ulcers in 27.7% and discoid rash in 3.9%). This was followed by haematological involvement in 57.7%, joint involvement in 26.9%, serositis in 15.4% and cerebral involvement in 14.6%.

In Hong Kong, prolonged fever was the most common extrarenal manifestation (55%). Fever was unfortunately not captured in our database. The other common features were malar rash, polyarthritis and haematological involvement.⁽⁸⁾

4.11.3: Classification of paediatric lupus nephritis

All renal biopsies were reviewed and classified according to WHO or ISN/RPS Classification. Class-IV or V+IV lupus Nephritis was found in 96 (65.7%) patients. Less frequent findings were class-III or V+III (17.1%), II (7.5%), V or V+II (6.9%) and VI (1.4%) lupus nephritis (Table 4.11.3). Hong Kong reported 54% in class IV.⁽⁸⁾ Thailand reported 48.8% in class IV and 30.5% in class II.⁽⁹⁾

Table 4.11.3: Classification of paediatric lupus nephritis

WHO/ISN /RPS Class	Number	%
Class I	0	0
Class II	11	7.5
Class III or V+III	25	17.1
Class IV or V+IV	96	65.7
Class V or V+II	10	6.9
Class VI	2	1.4
Unknown	2	1.4
Total	146	100

4.12: Renal outcome

Of the 579 patients biopsied, 44 children were reported to the Malaysian Dialysis and Transplant registry with end stage renal disease⁽¹⁰⁾ FSGS was the most common known cause of end stage renal disease accounting for 36.4%. This was followed by lupus nephritis (11.4%), systemic vasculitis (11.4%), post-infectious GN (9.1%) and advanced glomerulosclerosis (6.8%). Two patients with minimal change and one patient with acute tubular necrosis progressed to end stage renal disease (Table 4.12).

Table 4.12: Causes of end stage renal disease in children who underwent renal biopsy

Causes	Number	%
FSGS	16	36.4
Lupus nephritis	5	11.4
Systemic vasculitis	5	11.4
Post-infectious GN	3	6.8
Advance glomerulosclerosis	3	6.8
HUS/TTP	2	4.5
Membranoproliferative GN	2	4.5
Minimal change	2	4.5
IgA nephropathy	2	4.5
Mesangial proliferative GN non-IgA	1	2.3
Acute tubular necrosis	1	2.3
Chronic interstitial nephritis	1	2.3
Unknown	1	2.3
Total	44	100

4.13: Biopsy failure and complication

4.13.1: Risk factors for biopsy failure

Thirty-four out of the 640 (5.3%) renal biopsies were deemed to be inadequate for diagnosis.

There was no significant difference in success of renal biopsy with regards to age, real time ultrasound guidance and previous failed biopsy. This is probably because of the small number of failed renal biopsies (Table 4.13.1).

Table 4.13.1: Risk factors for biopsy failure

Factors	N	No of failure	Risk ratio	95% CI	p Value	
Age (years)	≤2	23	0	-	-	
	3-≤5	98	1	0.79	(0.26, 2.41)	0.68
	6-≤10	186	0	1.40	(0.66, 2.94)	0.38
	10-14 (ref*)	333	7	1.00	-	-
Methods	No real-time guided ultrasound	300	2	1.22	(0.45, 3.34)	0.70
	Real-time guided ultrasound (ref*)	86	6	1.00	-	-
Previous biopsy	Previous failed biopsy	8	4	3.18	(0.31, 32.4)	0.33
	Successful biopsy (ref*)	93	4	1.00	-	-

4.13.2: Complications

As shown in table 4.13.2, complications were reported in 5.4% of biopsies. The most common complication was gross haematuria, which occurred in 4.5% biopsies. Blood transfusion was needed in 1 patient. Six patients had perirenal haematoma. There were no cases of infection or arteriovenous fistula reported. None of the patients needed either surgical or radiological intervention. There were no cases of loss of kidney or death in association with biopsy procedure.

United Kingdom reported complications rate of 12%.⁽²⁾ Macroscopic haematuria was recorded in 7%. One patient required a single blood transfusion. The overall complication rate in Japan was 5.8%. Gross haematuria occurred in 2.7% and large perirenal hematoma in 0.9% of cases.⁽³⁾

Table 4.13.2: Frequency of complication

	Number	%
Total Number of biopsies	640	
Total Number of complication	38	5.4
Type of complication		
Gross haematuria	32	4.5
Perirenal collection/ haematoma	6	1.0
Infection	0	0
Arteriovenous malformation	0	0
Hypotension	0	0
Others	3	0.5
Unknown	1	0.2

4.13.3: Risk factors for complication

The risk of complication post renal biopsy was higher in those who had renal failure requiring dialysis and lower in those who had less than 2 passes of the biopsy needle. Age, hemoglobin level, lupus nephritis and needle size were not found to have significant impact on complication rate (Table 4.13.3).

Table 4.13.3: Risk factors for complication

	Factors	N	No of complication	Hazard ratio	95% CI	p value
Age (years)	≤2	23	1	0.85	(0.10,6.90)	0.88
	>2-≤5	98	9	1.80	(0.77,4.22)	0.18
	>5-≤10	186	9	0.86	(0.38,1.96)	0.72
	>10 (ref*)	333	19	1.00		
Requirement for dialysis	Renal failure needed dialysis	59	10	2.41	(1.10,5.28)	0.03
	Renal failure not needed dialysis (ref*)	519	28	1.00		
	Unknown ^a	62	0			
Creatinine clearance	<15 ml/min/1.73m ²	51	6	2.12	(0.78,5.76)	0.14
	15-<30 ml/min/1.73m ²	42	2	0.79	(0.17,3.60)	0.76
	30-<60 ml/min/1.73m ²	102	4	0.60	(0.20,1.83)	0.37
	60-<90 ml/min/1.73m ²	110	7	1.22	(0.49,3.04)	0.68
	≥90 ml/min/1.73m ² (ref*)	335	19	1.00		
Hemoglobin (Hgb) level	Hb ≤8g/dL	20	1	1.04	(0.13,8.49)	0.97
	Hb >8-≤10g/dL	122	8	0.98	(0.43,2.24)	0.97
	Hb ≥11g/dL (ref*)	482	29	1.00		
	Unknown ^b	16	0	-	-	-
Biopsy method (Realtime vs not)	Not realtime US guided	86	10	0.62	(0.28,1.36)	0.24
	Realtime US guided (ref*)	300	23	1.00		
	Unknown ^c	254	5	-	-	-
Biopsy method (Plug vs non-plug)	Plug biopsy *	5	0			
	Not plug biopsy (ref*)	361	32			
	Unknown ^d	274	6	-	-	-
SLE	SLE	163	8	0.70	(0.31,1.59)	0.40
	Non SLE (ref*)	477	30	1.00		
Needle size	14G	5	0	-	-	-
	16G (ref*)	383	36	1.00		
	18G	49	1	0.18	(0.02,1.37)	0.10
	Unknown ^e	203	1	-	-	-
Number of passes	Number of pass ≤2	250	16	0.47	(0.23,0.95)	0.04
	Number of pass 3-≤4 (ref)	144	18	1.00		
	Number of pass ≥ 5	17	3	1.92	(0.48,7.63)	0.36
	Unknown ^f	229	1	-	-	-

* Not able to do analysis due to the small sample size

a No information on renal failure needed dialysis for biopsy procedure data

b No information on haemoglobin (Hgb) level for biopsy procedure data

c No information ultrasound biopsy for biopsy procedure data

d No information on plug biopsy for biopsy procedure data

e No information on needle size for biopsy procedure data

f No information on number of passes for biopsy procedure data