Ultrasound-guided core biopsy in the diagnosis of lymphoma of the head and neck. A 9 year experience

¹C BURKE, MBChB, MRCS, ¹R THOMAS, MBBS, MRCP, ¹C INGLIS, MBBS, ¹A BALDWIN, MBBS,
²K RAMESAR, MRCPATH, ³R GRACE, FRCP, FRCPATH and ¹D C HOWLETT, MRCP, FRCP

¹Department of Radiology, ²Department of Pathology and ³Department of Haematology, Eastbourne District Hospital, East Sussex, UK

Objectives: This retrospective study aimed to evaluate the diagnostic utility of ultrasound-guided core biopsy (USCB) in lymphoma of the head and neck, in particular whether core biopsy can provide sufficient diagnostic information for definitive treatment.

Methods: All lymphomas diagnosed in the head and neck at Eastbourne General Hospital between January 2000 and June 2009 were identified. Radiology and pathology reports were reviewed and the diagnostic techniques recorded. The type of biopsy (fine needle aspiration, needle core, surgical excision biopsy) used to establish a diagnosis sufficient to allow treatment, i.e. the "index" diagnostic technique, was identified. Previous inconclusive or inadequate biopsies were noted. Pathology reports based on USCB were graded 0–3 according to diagnostic completeness and ability to provide treatment information.

Results: Of 691 overall cases of lymphoma diagnosed over the 9 year period, 171 different patients presented with lymphoma in the head and neck. Of these 171, 83 had USCB biopsy during diagnostic work up. 60 were regarded as grade 3 where a confident diagnosis of lymphoma was made. In seven patients, clinical management proceeded on the basis of a suggestive (grade 2) pathology report without surgical excision, and these were therefore also included as "index" biopsies. Overall therefore, 67/83 core biopsies (81%) provided adequate information to allow treatment. Surgical excision biopsy was the index modality in 104 cases.

Conclusion: In the majority of cases USCB is adequate for confident histopathological diagnosis avoiding the need for surgical excision biopsy in cases of suspected head and neck lymphoma.

Received 17 November 2009

Revised 10 May 2010

Accepted 15 June 2010

DOI: 10.1259/bjr/60580076

© 2011 The British Institute of Radiology

Enlargement of head and neck lymph nodes is a common presentation of malignant lymphoma, and accurate investigation is of great importance in patient management. Tissue sampling is required to establish a diagnosis [1, 2], and in order to commence adequate oncological therapy, biopsy specimens must allow not only diagnosis but also subclassification of lymphoproliferative disease [3–6].

Traditionally, lymphoma in the head and neck has been diagnosed by surgical excision biopsy [2, 5, 7]; however, in recent years there has been a trend towards diagnosing and even subclassifying lymphomas via less invasive techniques, in part related to advances in the ability of pathologists to make accurate diagnoses from small specimens as a result of advances in cytopathological and immunohistological techniques [2, 3, 8, 9].

Ultrasound-guided core biopsy (USCB) is cheaper, less invasive and associated with reduced morbidity, and there is increasing evidence that USCB can sample sufficient tissue for subclassification of lymphoma with immunohistochemical staining [1, 10, 11]. Several studies have now shown that core biopsy can guide management

of lymphoma without requirement for surgical excision biopsy [1, 2, 10, 11], which is of particular relevance to elderly people and those with multiple comorbidities.

We set out to evaluate the role of this technique in the specific setting of lymphoma of the head and neck, as management and diagnosis of neck masses is a controversial area. In particular, we aimed to clarify whether USCB can make a diagnosis of lymphoma and provide the necessary information for further management.

Methods and materials

All patients with lymphoma, including Hodgkin's disease, diagnosed at Eastbourne District General Hospital between January 2000 and June 2009 were identified by a Systematized Nomenclature of Medicine (SNOMED) search of the APEX pathology computer system using morphology codes for both Hodgkin's disease and non-Hodgkin's lymphoma (NHL). Radiology reports, imaging (where available) and patient records were also reviewed. The subgroup of lymphomas diagnosed in the head and neck was selected using both topography codes and manual review of the histopathology database. Location of biopsy, the "index" biopsy modality (i.e. the biopsy technique giving the definitive diagnosis: fine needle

Address correspondence to: Dr Christopher Burke, Department of Radiology, Eastbourne District Hospital, Kings Drive, East Sussex BN21 2UD, UK. E-mail: drchristopherburke@hotmail.com

aspiration (FNA), core or surgical excision) along with any previous or subsequent histology were documented.

The decision to perform core biopsy as opposed to excision biopsy was made among the clinical team, surgeon and radiologist. Biopsies were usually performed on an outpatient basis under local anaesthesia. A pre-procedure coagulation screen was not routinely performed. Core biopsy was performed without a pathologist present using real-time ultrasound guidance and a spring-loaded automated biopsy gun with side notch needles (length 10 cm, diameter 14–18 gauge). Multiple specimens from single or multiple nodes may be obtained depending on the quality of core specimen as assessed by inspection; however, the number of passes and size of lesions were not recorded in all instances. Tissue cores were preserved in formalin for histopathological examination. Histopathological reports had been issued by several pathologists working at our institution, including KR, with an interest in lymphoma.

The following data items were collated from histology and radiology reports:

- the exact location of the biopsy (e.g. thyroid, lymph node, major salivary gland);
- type of biopsy (FNA, needle core, excision biopsy) used to establish a conclusive diagnosis (index diagnostic technique);
- size of needle for core biopsies;
- the size of lesion, presence of necrosis and number of passes were also recorded where documented;
- whether there were previous inconclusive or inadequate biopsies; and
- type and subtype of lymphoma.

The diagnostic yield of core biopsies, FNA and surgical excision biopsies were graded:

- Grade 0 = insufficient sample for diagnosis.
- Grade 1 = equivocal where the pathologist was unable to differentiate reactive hyperplasia from lymphoma and excision was recommended.
- Grade 2 = consistent with lymphoma but a further diagnostic technique recommended for grading and typing purposes.
- Grade 3 = fully diagnostic for lymphoma and sufficient information obtained for grading and typing purposes to allow instigation of treatment.

Lymphomas were subtyped as follows:

1. Hodgkin's disease (all types);
2. diffuse large B-cell NHL (high-grade large B-cell NHL/high-grade B-cell (T-cell-rich B-cell NHL));
3. low-grade B-cell NHL unspecified;
4. MALT (mucosa-associated lymphoid tissue) NHL and marginal zone NHL;
5. mantle cell NHL;
6. follicular NHL (follicle centre cell NHL);
7. small lymphocytic NHL;
8. lymphoplasmacytic NHL;
9. anaplastic NHL;
10. peripheral T-cell NHL;
11. Burkitt's lymphoma.

Data from January until June 2009 were included in the results but excluded from the graphs as they represented only a partial year and would be visually misleading.

Results

A total of 691 different patients with lymphoma from all locations were identified between January 2000 and June 2009. Of these, 171 presented in the head and neck and 83 underwent USCB as part of their diagnostic pathway. Core biopsies had been performed by the same consultant radiologist (DCH), with over 12 years of head and neck imaging experience. The age range of patients who underwent core biopsy was 25–92 years (mean age 69 years). The range undergoing surgical excision biopsy was 22–79 years (mean age 62 years). The size of lesions ranged from 0.8 to 7 cm, although in 40% of cases size could not be recorded as this was not included in the report and the images were not available for review. Data relating to the internal architecture of nodes were only available in 50% of cases, with the presence of necrotic/cystic elements within nodes reported in 6 of these cases. The number of passes ranged from 1 to 7 (mean 4) although these data were only recorded in 53%.

Out of a total of 83 core biopsies, 60 provided adequate tissue for the pathologist to make a definitive diagnosis (grade 3) and a further 7 patients were treated on the pathology report consistent with lymphoma (grade 2) without proceeding to a further diagnostic technique. Therefore, core biopsy was the index modality for diagnosis in these cases 67/83 (81%) (Table 1). The remaining five patients with a grade 2 core underwent surgical excision biopsy, which was their index biopsy. There was one false-negative USCB from 2003 (reporting reactive change); however, clinical suspicion had led to a surgical excision that showed a diffuse B-cell lymphoma.

Six USCB reports could not distinguish between reactive and low-grade lymphoma (grade 1), all of which went on to have surgical excision confirming lymphoma. Four core biopsies contained insufficient tissue for assessment (grade 0). Three were later confirmed by surgical excision and one patient had a second 14-G core biopsy that was diagnostic following initial non-diagnostic 18-G biopsy (Table 1).

There was variation in the diagnostic yield for different types of lymphoma as shown in Table 2 (see also Table 4). Notably, 31/37 (84%) of diffuse large B-cell lymphomas were conclusively diagnosed on needle core biopsy (grade 3) but only 8/16 (50%) of Hodgkin's disease cases.

Of the seven (grade 2) cores suggestive of lymphoma that were managed without a further diagnostic technique and therefore still regarded as "index", three cores were suggestive of diffuse large B-cell lymphoma, one of low-grade B-cell NHL, two had cores suggesting follicular NHL and one of marginal zone NHL.

In 104 cases the index biopsy was an excision specimen. 14 surgical excision biopsies had had a previous non-diagnostic core biopsy. There was one non-diagnostic surgical excision biopsy (grade 0) due to severe crush artefact which went on to have a repeat excision biopsy (Figure 1).

Table 1. Grading of diagnostic completeness by modality

Grade	Index/total no. of core biopsies	Index/total no. of surgical biopsies	Total no. of fine needle aspirations
False-negative	1	0	1
0	4	1	7
1	6	0	10
2	12	0	15
3	60	104	0
Index/total	83	105	33

There were 33 FNAs during work up, none of which were index specimens (Figure 1). 7 FNAs failed to provide an adequate sample for analysis (grade 0) and 10 of the FNAs could not differentiate the cause of lymphoid proliferation (grade 1) (Table 1). There was one false-negative FNA reported as squamous cell carcinoma, which went on to subsequent surgical excision owing to clinical concern and was found to be a small lymphocytic lymphoma.

The remaining 15 FNAs suggested probable lymphoma (grade 2), but there was insufficient material to allow initiation of treatment. Of these FNAs, the lymphoma subtypes were later found to be three diffuse large B cell, three low-grade B cell, one peripheral T cell, three follicular centre cell, two low-grade MALT, one mantle zone and two cases of Hodgkin's disease.

In total, 27 FNAs went on to subsequent surgical excision biopsy and 6 went on to core biopsy. Of the six that proceeded to core biopsy, five were grade 3 and one was grade 2; therefore, all were positive for lymphoma.

The vast majority of biopsies came from cervical lymph nodes with a substantial minority from parotid masses (Table 3).

The total number of USCB increased year on year between 2000 and 2008. The number of FNAs and surgical excision biopsies decreased between 2005 and 2008 (Figure 1).

The proportion of fully diagnostic index core (grade 3) biopsies increased with time between 2000 and 2008 compared with equivocal cores either grades 1 or 2 (Figure 2).

Of the 22 cores graded 0–2, only 2 were performed with a 14-G needle (Figure 2). 20 had been performed

with an 18-G needle. Reasons for not using the 14-G biopsy needle included a target in the thyroid or salivary glands, small lesions and location near a vessel with poor accessibility.

Therefore, there was an increasing diagnostic yield with larger size of core biopsy needle (Table 4). Of the total cores performed with a 14-G needle, only 11% (2/18) were insufficient or equivocal compared with 31% with 18 G (20/64), excluding the 1 false-negative core. No significant complications were identified in any patients.

Discussion

Lymphoma has traditionally been diagnosed by surgical excision biopsy of an involved node, and this technique has represented the "gold standard" for diagnosis [2, 7, 8]. Operative node excision does however require input of surgical, nursing, anaesthetic and theatre staff, adding considerable cost as well as anaesthetic and surgical risks [12]. For these reasons, alternative techniques have been tried to obtain tissue for diagnosis, including FNA and more recently core biopsy.

FNA produces a cytological preparation, which allows cell identification to some degree but no ability to assess tissue architecture, and, in the district general hospital setting, no opportunity for immunohistochemistry [13]. These last two aspects are critical to accurate lymphoma diagnosis [14–16]. Immune techniques on cytological preparations and flow cytometry may be available in specialised centres. These limitations of FNA are borne out in our data where none of the 33 FNAs were fully diagnostic.

Core biopsy using ultrasound guidance is now a well-established technique widely used in sampling head and neck masses. It represents an alternative approach to the established ways of tissue sampling and provides an intermediate step between FNA and surgical excision biopsy. USCB can be performed under local anaesthetic, requiring only an ultrasound machine, a radiologist and nurse. It is performed as an outpatient, usually takes less than half an hour and has a good safety profile. Core biopsy is regarded as being particularly useful in elderly people and in those with multiple comorbidities. In our series, the mean age of patients undergoing core biopsy

Table 2. Diagnostic accuracy of core biopsy for each subclassification of lymphoma

	False-negative	Grade 0	Grade 1	Grade 2	Grade 3	Total
Hodgkin's disease (all types)			5	3	8	16
Diffuse large B-cell NHL	1	1	1	3	31	37
Low-grade B-cell NHL unspecified				1	4	5
Mantle cell NHL		1		1	1	3
Follicular NHL (follicle centre cell)		1		3	7	11
Marginal zone and MALT NHL (mucosa-associated NHL)		1		1	8	10
Small lymphocytic NHL						
Lymphoplasmocytic NHL						
Anaplastic NHL						
Peripheral T-cell NHL					1	1
Burkitt's lymphoma						
Total	1	4	6	12	60	83

MALT, mucosa-associated lymphoid tissue; NHL, non-Hodgkin's lymphoma.

Figure 1. The variation in the number of biopsies performed per modality between 2000 and 2009. FNA, fine needle aspiration.

was not markedly older than the surgical excision group (69 vs 62, respectively). Another advantage of USCB over surgical resection is that the lymph node is left in place, allowing monitoring of the therapeutic response [8].

There have been several papers demonstrating the excellent diagnostic yields from USCB from the parotid gland [17] and cervical lymph nodes [1, 10, 18]. Breast and liver USCB are well established, but the technique has only relatively recently become established in the salivary glands.

Concerns have been raised regarding the routine use of USCBs, specifically in lymphomas of the head and neck, as much of the current classification of lymphomas hinges on the detection of particular architectural patterns that may not be well represented in tiny needle biopsy specimens. Moreover, partial involvement of a lymph node by lymphoma makes sampling error possible, in which the needle biopsy may reach only the uninvolved portion of the node [19]. However, there remains a growing body of evidence to support its use. In 2009 Pfeiffer and colleagues reported 100% success in obtaining high-quality tissue cores. Indeed, they noted the target lymph node was correctly targeted, 41 of their 45 patients; in these 41 patients there were no false-positives or negatives results recorded and full subclassification of the disease with prompt institution of therapy was possible in 92.3% of the lymphoma patients [20].

Ultrasound guidance allows direct needle visualisation to avoid adjacent structures, and also ensures that the tip of the biopsy needle traverses the lesion without penetrating deep to it. Multiple areas from a mass can be sampled and non-palpable disease can be visualised and biopsied. Necrotic areas can be avoided and sampling of solid parts of complex lesions can be ensured.

Core biopsy produces a histological preparation which allows cell identification, some assessment of tissue architecture (particularly in larger gauge biopsies) and immunohistochemistry. These advantages greatly

improve the diagnostic yield with conclusive diagnosis achieved on 81% of needle cores in our series.

Within our data there was a trend towards improvement in diagnostic yield over the time period surveyed. This is multifactorial but probably reflects increasing confidence of histopathologists in making a diagnosis on core biopsies, as well as improvements in immunohistochemistry (better monoclonal antibodies and automated immunostaining) which occurred in our institution during this time period.

Early studies [21] suggested that core biopsy could only fully classify lymphoma in 38–51% of cases. However, some of these studies were carried out before the advent of most of the currently available monoclonal antibodies [21]. More recent work has suggested full subclassification of the disease with prompt institution of therapy was possible in 92.3% of the lymphoma patients [20].

Our results accord with the more recent studies [4, 20, 22] that achieved subclassification in 72–96% of cases. They also correlate with the data of Vandervelde et al [10] reported in 2008 with 51 head and neck lymphomas where 67% of core biopsies were fully diagnostic for treatment purposes.

A grade 1 core biopsy (equivocal), although not diagnostic, may nonetheless provide clinically useful information, as it indicates that the lesion, although equivocal with regard to exact histology, is lymphoid in nature, thus allowing exclusion of some important causes of head and neck lumps, *e.g.* metastatic carcinoma. It can also guide the need for either larger gauge core or surgical excision biopsy. A grade 2 core biopsy (suspicious of lymphoma) may provide sufficient information for treatment in elderly and frail patients and therefore spare them the risks associated with excision biopsy.

Variation in diagnostic yield between lymphoma subtypes has previously been recognised and our results correlate with those of Li et al [23] in showing a particular difficulty in the diagnosis of Hodgkin's disease on core biopsy. This probably reflects a greater heterogeneity in

Table 3. The location and type of biopsies. The number of index vs total biopsies is shown

	Core (index/total)	Surgical excision (index/total)	FNA (index/total)
Cervical lymph node	50/64	92/93	0/30
Parotid gland	14/16	7/7	0/3
Submandibular gland	0/0	4/4	0/0
Thyroid	2/2	0/0	0/0
Masseter	1/1	0/0	0/0
Total	67/83	103/104	0/33

FNA, fine needle aspiration.

Figure 2. The increasing proportion of grade 3 core biopsies with time.

histological appearance across the lymph node in Hodgkin's disease, with the consequent risk of sampling variation and the chance that critical features such as Reed–Sternberg cells might not be present in the core [2, 9, 24]. We found a variation in the diagnostic yield for different types of lymphoma, with 31/37 (84%) of diffuse large B-cell lymphomas conclusively diagnosed on needle core biopsy but only 8/16 (50%) of Hodgkin's disease cases. Sklair-Levy et al [2] reported that image-guided cutting edge needle biopsy was diagnostic in 59/69 (85.5%) of NHL patients and in 30/38 (78.9%) of Hodgkin's disease patients. We agree with Pfeiffer and colleagues [11, 20] that more information is needed, particularly in this lymphoma subtype. In contrast, there was a high sensitivity for diffuse large B-cell lymphoma, the most common subtype, where there is a diffuse, fairly uniform population of lymphomatous cells.

In view of these findings, USCB is now the method of choice for neck lump biopsy at our institution with the proviso that in negative core biopsy cases where the clinical and imaging findings suggest lymphoma (particularly Hodgkin's disease) we maintain a low threshold for proceeding to excision biopsy.

A notable finding in our study was that 14-G biopsies (where these could be taken) achieved a higher diagnostic yield than 18-G biopsies (89% *vs* 68%), although this is based on a small number of cores. This diagnostic improvement probably relates to an enhanced ability to see important architectural features on histology and reduced sampling variation in the wider gauge biopsies, and suggests that where possible the larger gauge needle should be used. It does however need to be borne in mind that larger gauge biopsy has been reported to be associated with increased risk of tumour seeding [25], an area of particular importance in the parotids. Pfeiffer and colleagues recommended to reduce the risk of missing the pathological area in a heterogeneously involved lymph node, or hitting a necrotic area, by using not too small cutting needles (≥ 16 -G). There are certainly locations where 18-G needles are safer, such as within the parotid and thyroid

glands and near vessels. This effect of core biopsy gauge should also be borne in mind when the results of different studies on this topic are compared. Also, increasing number of passes may improve diagnostic yield; however, this was only recorded in 53% of our patients.

Conclusion

With 83 core biopsies, this is the largest case series of lymphomas specifically presenting in the head and neck to our knowledge in the literature to date. With increasing recognition and acceptance of this minimally invasive technique by histopathologists and clinicians, we feel that USCB will increasingly form the key diagnostic investigation in patients with suspected head and neck lymphoma and is particularly useful in elderly people and those with comorbidities. Diagnostic yields may be improved using larger bore needles and increasing number of passes, and the technique is likely to be of similar utility in the axilla, groin and other superficial areas previously the domain of surgical biopsy.

References

1. Screatton NJ, Berman LH, Grant JW. Head and neck lymphadenopathy: evaluation with US-guided cutting needle biopsy. *Radiology* 2002;224:75–81.
2. Sklair-Levy M, Amir G, Spectre G, Lebensart P, Applbaum Y, Agid R, et al. Image guided cutting needle biopsy of peripheral lymph nodes and superficial masses for the diagnosis of lymphoma. *J Comput Assist Tomogr* 2005;29: 369–72.
3. Agid R, Sklair-Levy M, Bloom AI, Lieberman S, Polliack A, Ben-Yehuda D, et al. CT guided biopsy with cutting edge needle for the diagnosis of malignant lymphoma: experience of 267 biopsies. *Clin Radiol* 2003;58:143–7.
4. Pappa VI, Hussain HK, Reznick RH, Whelan J, Norton AJ, Wilson AM, et al. Role of image-guided core needle biopsy in the management of patients with lymphoma. *J Clin Oncol* 1996;14:2427–30.
5. de Kerviler E, Guermazi A, Zagdanski AM, Meignin V, Gossot D, Oksenhendler E, et al. Image guided core needle biopsy in patients with suspected or recurrent lymphomas. *Cancer* 2000;89:647–52.
6. Ben-Yehuda D, Polliack A, Okon E, Sherman Y, Fields S, Lebensart P, et al. Image guided core needle biopsy in malignant lymphoma: experience with 100 patients that suggests the technique is reliable. *J Clin Oncol* 1996;14:2431–4.
7. Demharther J, Neukirchen S, Wagner T, Schlimok G, Bohndorf K, Kirchof K. Do ultrasound guided core needle

Table 4. Diagnostic yield with the two sizes of core biopsy needle used

Size of core	False –ve	Grade 0	Grade 1	Grade 2	Grade 3	Total
18 G	1	4	6	10	44	65
14 G		0	0	2	16	18
Total	1	4	6	12	60	83

- biopsies of lymph nodes allow for subclassification of malignant lymphomas? *Rofo* 2007;179:396–400.
8. de Kerviler E, de Bazelaire C, Mounier N, Matheiu O, Brethon B, Briere J, et al. Image guided core needle biopsy of peripheral lymph nodes allows the diagnosis of lymphomas. *Eur Radiol* 2007;17:843–9.
 9. Hehn ST, Grogan TM, Miller TP. Utility of fine needle aspiration as a diagnostic technique in lymphoma. *J Clin Oncol* 2004;22:3046–52.
 10. Vandervelde C, Kamani T, Varghese A, Ramesar K, Grace R, Howlett DC. A study to evaluate the efficacy of image-guided core biopsy in the diagnosis and management of lymphoma – Results in 103 biopsies. *Eur J Radiol* 2008;66:107–11.
 11. Pfeiffer J, Kayser G, Technau-Ihling K, Boedeker CC, Ridder GJ. Ultrasound guided core needle biopsy in the diagnosis of head and neck masses: indications, technique and results. *Head Neck* 2007;29:1033–40.
 12. Shaw JH, Rumball EM. Complications and local recurrence following lymphadenectomy. *Br J Surg* 1990;77:760–4.
 13. Lioe TF, Elliott H, Allen DC, Spence RA. The role of fine needle aspiration cytology (FNAC) in the investigation of superficial lymphadenopathy: uses and limitations of the technique. *Cytopathology* 1999;10:291–7.
 14. Demharter J, Muller P, Wagner T, Schlimock G, Haude K, Bohndorf K. Percutaneous core-needle biopsy of enlarged lymph nodes in the diagnosis and subclassification of malignant lymphoma. *Eur Radiol* 2001;11:276–83.
 15. Das DK. Value and Limitations of fine-needle aspiration cytology in diagnosis and classification of lymphomas: a review. *Diagn Cytopathol* 1999;21:240–9.
 16. Roh J, Lee Y, Kim J. Clinical utility of fine-needle aspiration for diagnosis of head and neck lymphoma. *Eur J Surg Oncol* 2008;34:817–21.
 17. Kesse KW, Majnaly G, Violaris N, Howlett DC. Ultrasound-guided biopsy in the evaluation of focal lesions and diffuse swelling of the parotid gland. *Br J Oral Maxillofac Surg* 2006;4:384–8.
 18. Howlett DC, Menezes L, Bell DJ, Ahmed I, Witcher T, Bhatti N, et al. Ultrasound-guided core biopsy for diagnosis of lumps in the neck: results in 82 patients. *Br J Oral Maxillofac Surg* 2004;1:34–7.
 19. Carbone A, Ferlito A, Devaney KO, Rinaldo A. Ultrasound-guided core-needle biopsy: is it effective in the diagnosis of suspected lymphomas presenting in the head and neck? *J Surg Oncol* 2008;98:4–5.
 20. Pfeiffer J, Kayser G, Ridder GJ. Sonography assisted cutting needle biopsy in Head and Neck for the diagnosis of lymphoma: Can it replace lymph node extirpation? *Laryngoscope* 2009;119:689–95.
 21. Erwin BC, Brynes RK, Chan WC, Keller JW, Phillips VM, Gedgaudas-McClees RK, et al. Percutaneous needle biopsy in the diagnosis and classification of lymphoma. *Cancer* 1986;57:1074–8.
 22. Zinzani PL, Colecchia A, Festi D, Magagnoli M, Larocca A, Ascani S, et al. Ultrasound-guided core-needle biopsy is effective in the initial diagnosis of lymphoma patients. *Haematologica* 1998;83:989–92.
 23. Li L, Wu QL, Liu LZ, Mo YX, Xie CM, Zheng L, et al. Value of CT-guided core needle biopsy in diagnosis and classification of malignant lymphomas using automated biopsy gun. *World J Gastroenterol* 2005;11:4843–7.
 24. de Larrinoa AF, Del Cura J, Zabala R, Fuertes E, Bilbao F, Lopez JJ. Value of ultrasound guided core biopsy in the diagnosis of malignant lymphoma. *J Clin Ultrasound* 2007;35:295–301.
 25. Roussel F, Dalion J, Benoxio M. The risk of tumour seeding in needle biopsies. *Acta Cytol* 1989;33:936–9.