NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of image-guided radiofrequency excision biopsy of breast lesions

Breast lumps may need to be sampled to test for cancer. This minimally invasive procedure involves a small incision and insertion of a probe which uses radiofrequency energy to cut through the breast internally, aiming to remove the lump along with a small area of surrounding tissue to test for cancer.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in January 2009.

Procedure name

- Image-guided radiofrequency excision biopsy of breast lesions

Specialty societies

- British Association of Surgical Oncology
- British Society of Interventional Radiology
- Royal College of Radiology (Breast Group).

Description

Indications and current treatment

Breast cancer

Breast cancer is the most common cancer in women in the UK. Traditionally, the most common clinical presentation is a lump or mass in the breast. However, patients within certain age groups may be diagnosed with breast cancer at an asymptomatic stage through the NHS Breast Screening Programme.

There are several types of breast cancer. Lobular carcinoma in situ (LCIS) and ductal carcinoma in situ (DCIS) are very early forms of non-invasive breast cancer in which the cancer cells are contained inside the lobes or ducts of the breast and have not spread into the surrounding breast tissue. Left untreated, it may develop into an invasive cancer, such as invasive ductal carcinoma (IDC).

Breast cancer is usually categorised into four stages and three grades. Stage 1 describes a tumour of less than 2 cm in diameter that has not spread to the axillary lymph nodes or any other organs. At stage 4, the tumour has spread to other parts of the body such as the lungs, liver or bones, and is known as ‘advanced’. Grade 1, or low-grade cancer, is slow growing and the tumour cells resemble normal cells. In grade 2, or intermediate-grade cancer, the cells are moderately differentiated and grow at a faster rate. Grade 3 or high-grade cancer is fast growing and the cells are poorly differentiated.

Benign breast lesions

Fibroadenomas are benign tumours, typically about 1 to 3 cm in length. They are usually painless, but some people may experience pain or tenderness.

Diagnosis and treatment

Diagnosis, to establish whether a tumour is malignant or benign, is a critical step in management. Diagnosis is based on clinical findings, imaging and tissue sampling. Tissue sampling is usually by fine needle aspiration for cytology, or by needle core biopsy for histology. Histology allows for differentiation between benign tumours such as fibroadenomas, and others such as non-invasive DCIS and invasive IDC. Open surgical biopsy or image-guided vacuum-assisted core biopsy may also be used to establish tumour type and grade.

Treatment depends on the type, stage and grade of the tumour.

What the procedure involves

The aim of this procedure is to reduce to achieve minimally invasive retrieval of an intact specimen for histological examination, while minimising the risk of

bleeding and haematoma formation. This procedure is not indicated currently for the therapeutic removal of known cancers unless there are no surgical options. Under local anaesthesia and image guidance, (usually stereotactic or real-time ultrasound imaging) a small incision of 6–8 mm is made in the breast to the subcutaneous tissue level and a wand-like instrument with a unipolar radiofrequency (RF) cutting tip to ease passage through the breast tissue is advanced to the site of the lesion.

Depending on the design of the wand, a few small probe wires and capturing arms are extended from the tip of the wand (using RF energy to dissect the tissue) to surround the lesion. The sample is withdrawn along the same track. Wands of various diameters can be used, depending on the diameter of lesion to be captured. Alternatively, a wand with an expandable RF cutting band at the tip is deployed. The band traverses the tissue surrounding the target lesion as the shaft of the wand is rotated and the excised sample is deposited into a collection bag. The wand is then extracted and the incision closed without sutures.

List of studies included in the overview

This overview is based on 810 lesions treated from two case series[(1),(2);] the total number of patients treated is not reported.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Efficacy

The efficacy of RF excision biopsy is reported in terms of its diagnostic accuracy. A case series of 742 breast lesions evaluated with RF excision biopsy found that positive samples were found in 23% (172/742) of lesions, of which 94% (162/172) were diagnosed as DCIS or IDC[(1)]. Of the 34 lesions identified as atypical ductal hyperplasia (ADH) identified after RF excision biopsy, 9.4% were false negatives, as subsequent histological examination of specimens obtained through conventional surgery to remove the lump indicated IDC or DCIS. Similarly, 5.2% of cases diagnosed as DCIS following RF biopsy were classified as IDC after surgical excision and biopsy of the surgical specimen.

A case series of 100 patients (106 fibroadenomas) diagnosed using RF excision biopsy reported that 93% (79/85) of patients showed no physical or imaging evidence of residual lesions at 4- to 6-month follow-up[(2)]. There were no conversions to open surgery and no patient required additional diagnostic or therapeutic procedures during the follow-up period.

Safety

There was no evidence available on oncological safety outcomes (e.g. tumour recurrence), beyond the false negative rates observed in the case series of 742 biopsies. The same study reported that infection occurred in <1% (1/742) of biopsies (resolved with oral antibiotics)[(1)]. There were no instances of bleeding or haematoma requiring additional procedures, and no reports of skin burns (follow-up period not reported).

A case series of 100 patients (106 lesions) reported that bleeding occurred in 2% (2/106) of excision procedures (controlled by conservative measures)[(2)]. The mean pain score during the procedure was <1 point on a visual analogue scale from 0 to 10 (0 = no pain, 10 = most severe pain).

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to image-guided RF excision biopsy of breast lesions. Searches were conducted of the following databases, covering the period from their commencement to 16th December 2008, and updated to 1st April 2009: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy).

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with breast lesions either presumed benign or suspected malignant.
Intervention/test	Image-guided radiofrequency excision biopsy
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Image-guided vacuum-assisted excision biopsy of benign breast lesions NICE interventional procedures guidance 156 (2006). Available from www.nice.org.uk/IPG156

Table 2 Summary of key efficacy and safety findings on image-guided radiofrequency excision biopsy of breast lesions

Abbreviations used: ADH, atypical ductal hyperplasia; DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma; RF, radiofrequency.

Study details	Key efficacy findings	Key safety findings	Comments
Sie A (2006)[1] **Case series** Country: USA Study period: Nov 2002 to Sept 2004 Study population: Women with primary diagnosis based on mammography of ADH or DCIS undergoing biopsy for microcalcifications. **n = 742 lesions (number of patients not reported)** Age: not reported; Sex: 100% female Inclusion criteria: 'Compressed' breast >2.5 cm, with mammograms showing microcalcifications. Technique: Biopsy using RF excision using 10- or 15-mm wand with stereotactic guidance. Aim of procedure to retrieve representative diagnostic specimens and not necessarily to remove the entire mammographic finding. **Follow-up: not reported** Conflict of interest: One author is shareholder in and consultant to manufacturer.	**Diagnostic findings** Positive malignant samples with RF excision biopsy were found in 23% (172/742) of lesions: DCIS in 15% (119/742), IDC in 6% (43/742) of lesions, invasive lobular carcinoma in 1% (6/742), and lobular carcinoma in situ in <1% (2/742). There was also one papillary carcinoma and one mucinous carcinoma. **False negative investigations (for malignancy or cancer beyond DCIS) at subsequent surgery** ADH: Number of cases diagnosed at biopsy: 34; Number of cancers diagnosed at surgery: 3 (IDC or DCIS); Under diagnosed: 9.4%; Excluded from analysis: 2 DCIS: Number of cases diagnosed at biopsy: 119; Number of cancers diagnosed at surgery: 6 IDC; Under diagnosed: 5.2%; Excluded from analysis: 4	**Complications** Infection occurred in <1% (1/742) of biopsies, which resolved with oral antibiotics (follow-up period not reported). There were no instances of bleeding, haematoma requiring additional procedures and no complaints of skin burning. A low level of RF-associated thermal artefact was seen along the periphery of most specimens 0.1 to 1 mm deep; however, this did not prevent definitive diagnosis in any sample.	Ten participating centres. The first 15 patients at each site were classified as training and are excluded from analysis. Retrospective case series. Study undertaken to calculate the underestimation of pathology in women with primary diagnosis of ADH or DCIS. Open surgical biopsy was recommended for all patients with ADH or DCIS, but it is not stated whether those with negative biopsy underwent surgical removal, potentially leading to underestimation of false-negative rates. Physicians at each institution used their own criteria for selecting lesions for biopsy. Six patients were not included in analysis between biopsy and surgery: 3 were lost to follow-up, 2 declined surgery, and 1 died. Authors state that underestimation rates may result from biopsy sampling error or interpretation error.

Abbreviations used: ADH, atypical ductal hyperplasia; DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma; RF, radiofrequency.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Fine R E (2006)[2] **Case series** Country: USA Study period: Apr 2004 to Nov 2005 Study population: Women with imaging-based previous diagnosed fibroadenoma: 77 with palpable mass (ultrasound visible), 13 with abnormal mammogram, and 10 with abnormal ultrasound. **n = 100 (106 lesions)** Age: 45 years (mean); Sex: 100% female. Inclusion criteria: Not reported. Technique: Under local anaesthesia (all but one patient), biopsy using 'Ovation' wand with stereotactic (n = 18) or ultrasound guidance (n = 82), via a 6- or 7-mm incision. Aim to completely excise the lesion.. **Follow-up: 4 to 6 months** Conflict of interest: Not reported.	**Operative success** The success of the procedure was defined as no imaging evidence of lesion recurrence. 93% (79/85) of patients showed no physical or imaging evidence of residual fibroadenoma at 4- to 6-month follow-up. There were no conversions to open surgery. No patient required additional diagnostic or therapeutic procedure during the follow-up period.	**Complications** No incision-related adverse events occurred. Mean pain score during the procedure was <1 point on a visual analogue scale of 0 to 10 (0 = no pain, 10= most severe pain). Bleeding occurred in 2% (2/106) of lesions and was controlled by conservative measures.	Retrospective series. All procedures undertaken by one clinician experienced in image-guided percutaneous biopsy methods. Specimens were evaluated by independent pathologists.

Validity and generalisability of the studies

- No randomised controlled trial evidence.
- Very few meaningful efficacy outcomes are reported.
- The indication of the patients included in the case series was very different between the two studies. The outcome measures that may be useful for patients treated for tumours with imaging-based diagnosis of fibroadenoma may vary considerably from those having biopsy for suspected malignant lesions.
- One of the studies did not report any information about false negative rates/diagnostic accuracy.
- It is not clear whether all patients received subsequent surgical biopsy per protocol, or only those who had a positive sample on RF biopsy.
- The inclusion criteria are not well defined in either study.
- The majority of the literature regarding RF techniques in breast cancer in general is for use as ablation rather than biopsy.

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr S Allen (Royal College of Radiologists), Mr D Crawford (British Association of Surgical Oncology), Mr P Forouhi (British Association of Surgical Oncology), Prof. R Mansel (British Association of Surgical Oncology), Dr R Wilson (Royal College of Radiologists).

- Three Advisers considered this procedure to be novel and of uncertain safety and efficacy. Two Advisers considered it to be a minor variation of an existing procedure.
- Key efficacy outcomes for this procedure when used for benign lesions include intact removal of the lesion, patient acceptability / cosmetic appearance. Additional outcomes when used in early breast cancer include delivery of an evaluable lesion for histology, local recurrence and survival.

- The standard comparator for this procedure would be no treatment (for benign lesions), open excision, mammatome excision, or tube-based en-bloc lesion excision.
- Adverse events known to Specialist Advisers or reported in the literature include haematoma, infection, skin burns, and failure to retrieve a specimen.
- Additional theoretical adverse events may include seeding of tumour cells along biopsy tract, haemorrhage, pain (temporary), failure to deliver a adequate sample, and fat necrosis due to thermal damage.
- The use of this procedure for removal of benign breast lesions with no significant malignant potential would be relatively uncontroversial. However, use as a treatment for early breast cancer would be highly controversial and could only be sanctioned after full evaluation in a randomised clinical trial.
- The safety (and more so efficacy) of this procedure as a therapeutic option for neoplastic lesions needs to be established.
- Individuals using the procedure will be familiar with image-guided excision techniques and existing facilities and skills would be transferable. Training may be required from a RF-experienced team.
- The procedure could be applied in a district general hospital setting by multidisciplinary breast cancer teams.
- Four of the five Advisers thought that, if found to be safe and efficacious, the procedure would be offered at a minority of sites, but at least 10.
- There are some concerns about heat destruction of the tissue being biopsied.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme identified a number of trusts performing the procedure but none responded to requests to gather patient commentary.

Issues for consideration by IPAC

- Non-English-language studies were excluded from the overview.
- Both benign and suspected malignant indications were included in the scope of this guidance.

References

1 Sie A, Bryan DC, Gaines V et al. (2006) Multicenter evaluation of the breast lesion excision system, a percutaneous, vacuum-assisted, intact-specimen breast biopsy device. Cancer 107: 945-949.

2 Fine RE and Staren ED. (2006) Percutaneous radiofrequency-assisted excision of fibroadenomas. American Journal of Surgery 192: 545-547.

Appendix A: Additional papers on image-guided radiofrequency excision biopsy of breast lesions

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

There were no additional papers identified.

Appendix B: Related NICE guidance for image-guided radiofrequency excision biopsy of breast lesions

Guidance	Recommendations
Interventional procedures	**Image-guided vacuum assisted excision biopsy of benign breast lesions. NICE interventional procedures guidance 156 (2006)** 1.1 Current evidence on the safety and efficacy of image-guided vacuum-assisted excision biopsy of benign breast lesions appears adequate to support the use of this procedure, provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 Clinicians wishing to perform this procedure should undergo training as recommended by the Royal College of Radiologists in 'Ultrasound training recommendations for medical and surgical specialties' (www.rcr.ac.uk/docs/radiology/pdf/ultrasound.pdf).
Technology appraisals	There is currently no NICE guidance related to this procedure
Clinical guidelines	There is currently no NICE guidance related to this procedure
Public health guidance	There is currently no NICE guidance related to this procedure

Appendix C: Literature search for image-guided radiofrequency excision biopsy of breast lesions

Database	**Date searched**	Version/files	**No. retrieved**
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	16/12/2008	Issue 4, 2008	0
Database of Abstracts of Reviews of Effects – DARE (CRD website)	16/12/2008	N/A	1
HTA database (CRD website)	16/12/2008	N/A	0
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	16/12/2008	Issue 4, 2008	1
MEDLINE (Ovid)	16/12/2008	1950 to November Week 3 2008	51
MEDLINE In-Process (Ovid)	16/12/2008	December 11, 2008	7
EMBASE (Ovid)	16/12/2008	1980 to 2008 Week 50	46
CINAHL (NLH Search 2.0)	16/12/2008	N/A	16
BLIC (Dialog DataStar)	16/12/2008	N/A	1
National Research Register (NRR) Archive	16/12/2008	N/A	0
UK Clinical Research Network (UKCRN) Portfolio Database	16/12/2008	N/A	0
Current Controlled Trials *meta*Register of Controlled Trials - *m*RCT	16/12/2008	N/A	0
Clinicaltrials.gov	16/12/2008	N/A	Radiofrequency of Breast Cancers in Non Surgical Patients Percutaneous Removal and Margin Ablation for Breast Cancer

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	(breast* adj3 (neoplasm* or metastasis* or cancer* or lump* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan*)).tw.
2	Fibroadenoma/
3	fibroadenoma*.tw.
4	exp Breast Neoplasms/
5	(breast* adj3 diseas*).tw.
6	Breast Diseases/
7	or/1-6
8	(breast* adj3 lesion* adj3 excision* adj3 system*).tw.
9	BLES.tw.
10	Biopsy/
11	Radio Waves/
12	radiowave*.tw.
13	(radio* adj3 frequenc*).tw.
14	radiofrequenc*.tw.
15	(radio* adj3 wave*).tw.
16	biops*.tw.
17	16 or 10
18	15 or 11 or 14 or 13 or 12
19	intact*.tw.
20	17 and 18
21	8 or 9 or 20
22	21 and 7
23	21 and 19
24	22 or 23
25	animals/
26	humans/
27	25 not (25 and 26)
28	24 not 27

29 from 28 keep 1-51