Assessment of microcalcifications with limited number of high precision macrobiopsies. Time to reconsider guidelines?

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Abstract

Up-right stereotactic assessment of microcalcification clusters with direct and frontal macrobiopsies was performed in a population of 46 women screened for breast cancer. Sensitivity of the procedure was 98% and calcifications were detected in 107 out of 148 tissue specimen (73%). This is the highest reported ratio so far. Interestingly the total number of cores inversely correlated with success rate suggesting that accuracy of the direct and frontal approach is high. 4 out of 46 women underwent surgery for malignancy indicating that 41 women escaped intervention with a mean follow-up of at least one year. Patient satisfactoriness is high in particular towards reported pain, fear and overall appreciation. No complications were seen. The data suggests that a lower number of macrobiopsies for microcalcifications could be acceptable with direct and frontal biopsy methods without reducing sensitivity. Lowering the number of biopsies can optimize surgical margin interpretation and reduce the number of biopsy related mastectomies. (Eur J Cancer Prev: Submitted)

Introduction

Clinical guidelines for microcalcification assessment propose the use of vacuum assisted biopsy (VAB) instead of tru-cut core needle biopsy under stereotactic guidance. Tru-cut biopsies are considered inappropriate because of the small tissue samples that exclude proper histopathological analysis[1]. But even for macrobiopsies at least six biopsies are recommended in order to reach optimal sensitivity. The lateral uptake of these needles requires a 360° biopsy to make sure that the intended cluster of microcalcifications is taken up in at least one of the samples. Some clinicians prefer to increase the number of biopsies to even more than 20. Technological improvements of the VAB devices with fast suction and cutting make this possible indeed. The stereotactic guided VAB procedure has been taken up in several guidelines for microcalcification assessment.

However, increasing the number of biopsies has clinical limitations. Multiple sampling of suspect lesions might result in an inability to assess free margins at the time of surgery leading to an increase in lumpectomy volume. For small breasts this might mean mastectomy. Disruption of architecture after VAB is well-known to facilitate clip migration[2], a sign that malignant cells migrate as well. In addition, hematoma formation may disperse cells to even larger volumes. VAB procedures limit breast conservative surgery in up to 30 % of the cases[3],[4],[5]. When multiple stereotactic macrobiopsies decrease the probability of breast preservation the important advantage of early detection, less mutilation, might be lost.

Negative surgical margins of 10 mm or greater remains one of the most important determinants for a successful treatment[6]. Positive surgical margins at lumpectomy can results from disease related factors as mammographic microcalcifications, larger tumour size, and multifocal tumours[7]. In a number of studies with limited amount of

stereotactic large-core needle biopsies there was however a greater frequency of tumour-free margins after local excision[8] and overall, combining benign and malignant lesions, the use of macrobiopsies might reduce the frequency of surgical interventions[9].

To safely reduce the number of macrobiopsies without decreasing sensitivity, direct and frontal biopsy systems have been developed with the purpose to improve targeting accuracy. In this procedure, microcalcifications are taken up at the tip of the device under stereotactic guidance and positioning of microcalcifications in the needle is confirmed before cutting takes place. The device navigation is under complete control of the operator in manual and automated version. The clinical usefulness of direct and frontal biopsy (Spirotome, Coramate) has been addressed in several previous publications[10],[11],[12].

This paper describes the independent single institute clinical results of microcalcification assessment by the Spirotome 10 Gauge.

Materials and methods

Patient population

Forty-six procedures for microcalcifications were performed in 46 women between October 2007 and August 2009. The recorded data was procedure identification number, date, starting time, end time, total time, total number of cores, number of cores with calcification, application of clip marker, histology, further management and complications. Complications were defined as prolonged stay in the hospital or need of additional clinical measures.

The number of cores was upon discretion of the operator and the clinical situation.

Instruments

All stereotactic guidance was made with an up-right mammography equipment (Mammomat, Siemens, Germany) supplemented with biopsy try according to the instructions of the manufacturer.

The biopsy was made by the Spirotome 10 Gauge (MedInvents, Belgium) according to the instructions of the manufacturer. In short, and after proper skin disinfection, skin and deep local anaesthesia, a cross incision in the skin is made of 2 times 5 mm. Then the trocar with cutting cannula is advanced under the skin by twisting the trocar up to the site of microcalcifications. The trocar is removed and the receiving needle with helix is inserted instead. The helix is navigated into the cluster of microcalcifications by clockwise rotation and under stereotactic controle. After position verification the sample is cut by the cutting cannula and removed. Multiple samples can be taken during one transdermal insertion. The presence of microcalcifications is evaluated by radiology of the specimen. Tissue fixation is prepared by immersion in formol 5 per cent.

Data reporting

Core biopsy diagnoses are classified according to the Non-operative Diagnosis Subgroup of the British National Health Service Breast Cancer Screening Programme (NHSBSP). B1 means unsatisfactory or normal tissue only; B2 Benign; B3 Lesion of uncertain malignant potential; B4 Suspicion of malignancy; and B5 malignant[13].

Patient acceptability with regard to fear and pain was recorded in a scale of 5 going from 1: no fear – pain; 2 slight; 3 equivocal; 4 moderate; and 5 severe.

Results

Procedural time

In this population of 46 patients with cluster of microcalcification on screening the average procedural time was 48 minutes (St dev 18 min) with a minimal time of 25 and a maximal time of 100 minutes. The procedural time trend was stable during the study period.

Number of cores with microcalcifications

The average number of cores taken was 3 (St dev 1,28) with a minimum of 1 and maximum 6. The distribution was 1 core in 2 patients, 2

cores in 13 patients, 3 cores in 15 patients, 4 cores in 8 patients, 5 cores in 5 patients and 6 cores in 3 patients.

The number of cores with microcalcifications per total number of cores is depicted in table 1. In a total of 148 cores 107 showed the presence of microcalcifications. There is a trend for accuracy towards lesser number of total cores.

Table 1: Number of microcalcification containing cores per total number of cores

Number of microcalcification containing cores/total cores	1 CORE TOTAL	2 CORES TOTAL	3 CORES TOTAL	4 CORES TOTAL	5 CORES TOTAL	6 CORES TOTAL
0 with microcalcification					1	
1 with microcalcification	2	2	1			1
2 with microcalcification		11	10	2		1
3 with microcalcification			4	2	2	
4 with microcalcification				4	2	
5 with microcalcification						1
6 with microcalcification						
	2	**13**	**15**	**8**	**5**	**3**

The false negative rate is 1 out of 46 patients (2%) indicating a success rate of 98%.

Histological verification

Histological analysis is depicted in table 2

Table 2: Histological reporting of microcalcification assessment

B1	3
B2	38
B3	1
B4	0
B5	4
TOTAL	46

Clinical follow-up

In 3 patients (B1, B1 and B3) a mammotome procedure was added. The diagnosis was confirmed in all three.

In 3 patients with proven invasive cancer 3 underwent mastectomy and 1 wide local excision. One patient with DCIS had mastectomy. The decision for mastectomy was institutional guidelines and was unrelated to the biopsy procedure.

Clip application

Fourteen patients had a clip placed at the site of biopsy (30%) while 31 had no clip at the end of the procedure (67%). The patient with no calcifications in 5 cores had no clip. Clip placement was judged on mammographic appearance of microcalcifications.

Patient acceptability and complication rate.

Fear and pain as well as overall impression were recorded in a 5 point score with 1 complete comfort to 5 severe discomforts. In 8 patients no score has been obtained. The distribution of the scores in 38 patients is indicated below (table 3). One patient fainted during the procedure. She had 2 cores removed while both had microcalcifications.

Table 3: Patient acceptability

Score	Fear	Pain	Overall
5	4	1	2
4	2	2	5
3	11	12	22
2	8	12	8
1	13	11	1
	38	38	38
Average	**2,4**	**2,2**	**2,9**

In no patient out of 46 a complication with regard to infection, haemorrhage or excessive pain was noted.

Discussion

The strength of this study is the precise selection of patients with a cluster of microcalcifications on mammography and the independency of the study towards manufacturers. All equipment was purchased and no financial support from the companies was requested. Due to the stringent selection criteria, the number of patients is moderate but reflects confidently accrual in a typical reference centre.

In contrast to common belief and contemporary guidelines on classical VABs, the number of macrobiopsies doesn't affect sensitivity (measured here as number of cores with microcalcifications per total number of cores – 72%). According to this data, less than 4 biopsies with the Spirotome provide sufficient material to establish a reliable diagnosis i.e. that microcalcifications are indeed in one or more samples per procedure. Sampling was guided by upright stereotactic biopsy, a widely available technique, and microcalcifications were found in 45/46 patients (98% success rate with an average of 3,2 specimen). In comparison, ultrasound-guided VAB of microcalcifications have a success-rate amounting to 71 per cent[14] and under stereotactic guidance up to 95% with a mean of 14 specimen per procedure[15,16]. The low costs of the biopsy instrument and the widely available up-right tables opens this procedure for all women at risk.

Of particular interest is the high number of cores with microcalcifications per procedure in the data, indicating that the procedure can be performed with high precision as well. To our knowledge, this is the highest score ever published and in line with the complete navigation control of the helix that localizes the biopsy site before cutting takes place. In addition, the data suggests that total manual control of the biopsy procedure improves the success rate.

The procedural time is in line with contemporary standards. Most of the time has been devoted to localization of microcalcifications and positioning of the patient. The biopsy step takes usually a fraction of total procedural time without exceeding 20 minutes. This is made possible through the lesser preparation time of the biopsy equipment that is available in a ready to use package.

The number of malignant specimen is 4 in a population of 46 patients. That is low compared to data from literature[15, 16] where up to 30 % of the patients with microcalcifications are diagnosed with malignancy. However, the number might well reflect the actual situation for a regional hospital at first referral without further selection of patients. The median follow-up time is over 1 year and no upgrading or false diagnoses were made so far. This is in line with the high number of microcalcification containing cylinders that constitute the basis of a representative histopathology.

Three out of 4 patients with malignancy underwent mastectomy. These mastectomies were planned in view of the institutional guidelines and are not secondary to difficulties in assessing the surgical margins. More important 41 out of 46 patients escaped surgery for microcalcifications in the breast.

Tissue markers or clips are vital in the follow-up of microcalcifications, in particular when

surgery is indicated. In this population of patients, clip application was judged necessary in 14 patients. There was no correlation between clip placement and histopathology indicating that risk assessment based on radiological characteristics of microcalcifications is rather unreliable. This is in line with conclusions from several other publications[17].

Patient acceptability was measured for fear, pain and overall appreciation. In all three questionnaires the Spirotome showed satisfactory levels of acceptance (below 3). Because fear scored higher in the discomfort scale compared to pain and because fear is an essential determinant of pain, a substantial improvement in comfort might be obtained by proper information of the patient before the procedure. No complication has been observed that needed prolonged stay or additional interventions. This is in line with literature where low complication rates have been observed for both micro- and macrobiopsies.

The data suggests that high-precision macrobiopsies don't need excessive numbers of cores to be representative leading to maximal probability for breast conserving treatments. Confirmation of these data with multicentric studies is necessary before implementation into a new standard is warranted but the findings are encouraging that improvements in macrobiopsy technology can provide women with microcalcifications a significantly higher chance to conserve the breast and improved cosmetics in case of malignancy.

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