AHRQ Comparative Effectiveness Review Surveillance Program

CER # 19:
Comparative Effectiveness of Core Needle Biopsy and Open Surgical Biopsy for Diagnosis of Breast Lesions

Original release date: December, 2009

Surveillance Report 1st Assessment: December, 2011
Surveillance Report 2nd Assessment: July, 2012

Key Findings, 1st Assessment:

- For Key Question 1, the conclusion regarding DCIS underestimation rate for stereotactically guided vacuum assisted CNB is possibly out of date, and information on the accuracy of MRI guided CNB is now available. Conclusions for accuracy of freehand automated gun CNB are out of date; however, this procedure is now rarely performed in the U.S.
- For Key Question 2, there may now be enough studies to conduct a meta-regression on the effect of characteristics of the lesion, patient, and provider on accuracy.
- For Key Question 3, experts felt the conclusion on number of surgical procedures required after biopsy was possibly out of date.

These findings were unchanged from the last assessment

Summary Decision

This CER's priority for updating is **Medium** (This is unchanged from the last assessment)

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Comparative Effectiveness of Core Needle Biopsy and Open Surgical Biopsy for Diagnosis of Breast Lesions

1. Introduction

Comparative Effectiveness Review (CER) # 19 was originally released in December 2009.[1] It was therefore due for a surveillance assessment in June, 2010. The Surveillance Program commenced in late summer 2010, and the first assessment of CER #19 was submitted in October, 2011. This second assessment was completed in July, 2012.

2. Methods

2.1 Literature Searches

We conducted a limited literature search using the identical search strategy used for the original report. This search included five high-profile general medical interest journals (Annals of Internal Medicine, British Medical Journal, Journal of the American Medical Association, Lancet, and the New England Journal of Medicine) and five specialty journals (American Journal of Roentgenology, Breast, Breast Journal, Pathology, and Radiology). The specialty journals were those most highly represented among the references for the original report. The first assessment search covered January, 2008 to October, 2011 and resulted in 244 titles. The second assessment search covered June, 2011 to June, 2012 and resulted in 32 titles. Appendix A includes the search strategy.

2.2 Study selection

In general we used the same inclusion and exclusion criteria as the original CER. However, the original CER excluded studies where sensitivity was not reported. We included articles where atypical ductal hyperplasia (ADH) and ductal carcinoma in situ (DCIS) underestimates were reported, as these issues were included in the key questions; some of these studies did not report overall sensitivity. The inclusion/exclusion criteria remained unchanged for the second assessment.

2.3 Expert Opinion

For the first assessment, we shared the conclusions of the original report with 13 experts in the field (including the original project leader, suggested field experts, original technical expert panel (TEP) members) for their assessment of the need to update the report and their recommendations of any relevant new studies. The EPC lead authors and five subject matter experts responded. Appendix C shows the questionnaire matrix that was sent to the experts. For

the second assessment, we reached out to the five experts with a modified matrix that included the experts prior responses. Two experts responded back.

2.4 Check for qualitative and quantitative signals

The authors of the original CER conducted several meta-analyses on the accuracy of various types of core needle biopsy (CNB) of breast lesions. When we identified new studies that reported accuracy rates outside the 95% confidence intervals, we considered the conclusion possibly out of date. More importantly, when we identified studies reporting accuracy or adverse events associated with a particular type of CNB where none previously existed, we considered the conclusion out of date.

2.5 Compilation of Findings and Conclusions

We constructed a summary table that includes the key questions, the original conclusions, the findings of the two new literature searches, the expert assessments, and any FDA warnings issued since the publication of the original CER. We categorized whether the conclusions need updating using a 4-category scheme:

- Original conclusion is still valid and this portion of the CER does not need updating
- Original conclusion is possibly out of date and this portion of the CER may need updating
- Original conclusion is probably out of date and this portion of the CER may need updating
- Original conclusion is out of date.

We used the following factors when making our assessments:

- If we found no new evidence or only confirmatory evidence and all responding experts assessed the CER conclusion as still valid, we classified the CER conclusion as still valid.
- If we found some new evidence that might change the CER conclusion, and /or a minority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as possibly out of date.
- If we found substantial new evidence that might change the CER conclusion, and/or a majority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as probably out of date.
- If we found new evidence that rendered the CER conclusion out of date or no longer applicable, we classified the CER conclusion as out of date. Recognizing that our literature searches were limited, we reserved this category only for situations where a limited search would produce prima facie evidence that a conclusion was out of date, such as the withdrawal of a drug or surgical device from the market, a black box warning from FDA, etc.

2.6 Determining Priority for Updating

We used the following two criteria in making our final conclusion for this CER:

- How much of the CER is possibly, probably, or certainly out of date?
- How out of date is that portion of the CER? For example, would the potential changes to the conclusions involve refinement of original estimates or do the potential changes mean some therapies are no longer favored or may not exist? Is the portion of the CER that is probably or certainly out of date an issue of safety (a drug withdrawn from the market, a black box warning) or the availability of a new drug within class (the latter being less of a signal to update than the former)?

3. Results

3.1 Search

1st assessment: 244 titles were identified from the literature searches covering January, 2008 to October, 2011. After title and abstract screening, 28 of these were selected for full text review. Twenty-two additional articles were reviewed at the suggestion of the experts. Nineteen studies were accepted and abstracted into an evidence table.[2-20]

2nd assessment: 32 titles were identified from the literature searches covering June, 2011-June, 2012. After title and abstract screening seven articles were selected for full text review. One expert suggested an article which was reviewed. One systematic review and four accuracy studies were accepted and added to the evidence table.[21-25]

Appendix B includes the cumulative data for the 24 included studies. The five new studies are bolded.

3.2 Expert Opinion

2nd assessment: Both experts who responded thought there was no new evidence for all three Key Questions.

3.3 Identifying qualitative and quantitative signals

In this CER we only checked for qualitative and quantitative signals. Table 1 shows the original key questions, the conclusions of the original report, the results of our first surveillance assessment (literature and drug database searches, experts' assessments, and our EPC's recommendations) and the results of our second surveillance assessment in July, 2012. In sum, the new studies and feedback did not change any of our December, 2011 recommendations. The priority for updating this report is medium and has remained unchanged since the prior assessment.

Table 1: Summary Table – July, 2012

Conclusions From CER	RAND Literature Search	FDA	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC	Conclusions of validity of CER conclusion(s)	
					Prior Assessment	**Cumulative Assessment**
Key Question 1: In women with a palpable or nonpalpable breast abnormality, what is the accuracy of different types of core-needle breast biopsy compared with open biopsy for diagnosis?						
Stereotactically guided vacuum-assisted core-needle biopsies (CNB) have a sensitivity of 99.2 percent (95-percent confidence interval [CI]: 97.9 to 99.7 percent). Strength of evidence: Low	**December 2011** - We found one new study of stereotactically guided vacuum assisted CNB that reported sensitivity; rate was 95.5% in 64 patients, using 11 gauge CNB (Wiratkapun, 2010). In addition, a recent meta-analysis (Yu, 2010) that pooled results from sterotactically and ultrasound guided vacuum assisted CNB reported a sensitivity rate of 98.1%. **July 2012** – Three new studies combined results for stereotactic and ultrasound guided CNB, so rate not calculable.	**December 2011 -** No new data. **July 2012** – No new data.	**December 2011** – All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011** - Conclusion still valid. **July 2012 -** Conclusion still valid.	**Up-to-date**	**Up-to-date**
Stereotactically guided vacuum-assisted core-needle biopsies have a DCIS underestimation rate of 13.0 percent (95-percent confidence interval [CI]: 11.1 to 15.1 percent). Strength of evidence: Low	**December 2011** - We found two new studies of stereotactically guided vacuum assisted CNB that reported DCIS underestimation rates of 19.2% (Salem, 2009) and 23.0% (Ho, 2008). In Yu's meta-analysis, the pooled rate was 11.2% in 12 studies of both stereotactically and ultrasound guided vacuum assisted CNB. Brennan (2011) conducted a meta-analysis of 52 studies reporting DCIS under-estimation in both stereotactically and	**December 2011 -** No new data. **July 2012** – No new data.	**December 2011** – All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011** - Conclusion is possibly out of date based on the much higher estimate reported in the Brennan (2011) meta-analysis. This portion of the CER may need updating. **July 2012 -** Conclusion possibly out of date.	**Possibly out-of- date.**	**Possibly out –of- date.**

Conclusions From CER	RAND Literature Search	FDA	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC	Conclusions of validity of CER conclusion(s)	
					Prior Assessment	Cumulative Assessment
	ultrasound guided CNB; rate was 23.9%. **July 2012** – Three new studies combined results for stereotactic and ultrasound guided CNB, so rate not calculable.					
Stereotactically guided vacuum-assisted core-needle biopsies have an ADH underestimation rate of 21.7 percent (95-percent confidence interval [CI]: 17.7 to 26.4 percent). Strength of evidence: Low	**December 2011** - We found four new studies of stereotactically guided vacuum assisted CNB that reported ADH underestimation rates of 18.2% (Salem, 2009), 19.8% (Kohr, 2010), 20.4% for 11 gauge and 21.6% for 9 gauge (Eby, 2009) and 50% (Wiratkapun, 2010). For stereotactic and ultrasound guided combined, rate was 20.9% in Yu's meta-analysis and 22.0% in a new study by Londero (2011). The unusually high rate in Wiratkapun, 2010, was conducted in Thailand; there were 6 cases of ADH of 64 lesions. **July 2012** – Three new studies combined results for stereotactic and ultrasound guided CNB, so rate not calculable.	**December 2011** - No new data. **July 2012** – No new data.	**December 2011** - All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011** - Conclusion is still valid. **July 2012 - –**Conclusion still valid.	**Up-to-date**	**Up-to-date**
Stereotactically guided automated gun core-needle biopsies have a sensitivity of 97.8 percent (95-percent	**December 2011** - No new studies. **July 2012** – No new studies on automated gun CNB.	**December 2011** - No new data. **July 2012** – No new data.	**December 2011** - All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed	**December 2011** - Conclusion still valid. **July 2012 -** Conclusion still valid.	**Up-to-date**	**Up-to-date**

Conclusions From CER	RAND Literature Search	FDA	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC	Conclusions of validity of CER conclusion(s)	
					Prior Assessment	Cumulative Assessment
CI: 95.8 to 98.9 percent). Strength of evidence: Low			conclusion is still valid.			
Stereotactically guided automated gun core-needle biopsies have a DCIS underestimation rate of 24.4% percent (95-percent CI: 18.0 to 32.1 percent). Strength of evidence: Low	**December 2011 -** No new studies. **July 2012** – No new studies on automated gun CNB.	**December 2011 -** No new data.	**December 2011 -** All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011 -** Conclusion still valid. **July 2012 -** Conclusion still valid.	**Up-to-date**	**Up-to-date**
Stereotactically guided automated gun core-needle biopsies have a sensitivity of 43.7% percent (95-percent CI: 35.7 to 51.7 percent). Strength of evidence: Low	**December 2011** - No new studies. **July 2012** – No new studies on automated gun CNB.	**December 2011** - No new data. **July 2012** – No new data.	**December 2011** - All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011** - Conclusion still valid. **July 2012 – Conclusion still valid,**	**Up-to-date**	**Up-to-date**
Ultrasound-guided vacuum-assisted core-needle biopsies have a sensitivity of 96.5 percent (95-percent CI: 81.2 to 99.4 percent). Strength of evidence: Low	**December 2011** - New studies of ultrasound-guided vacuum-assisted CNB included only high risk lesions described as either atypical, "borderline," or DCIS. Thus, overall sensitivity was not calculable. **July 2012** – Three new studies combined results for stereotactic and ultrasound guided CNB, so rate not calculable.	**December 2011** - No new data. **July 2012** – No new data.	**December 2011** - All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011** - Conclusion still valid. **July 2012 -** Conclusion still valid.	**Up-to-date**	**Up-to-date**

Conclusions From CER	RAND Literature Search	FDA	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC	Conclusions of validity of CER conclusion(s)	
					Prior Assessment	Cumulative Assessment
It was not possible to calculate the DCIS underestimation rate for ultrasound-guided vacuum-assisted core-needle biopsy. Strength of evidence: Insufficient	**December 2011 -** The only new studies reporting DCIS underestimation rate combined results for ultrasound and stereotactically guided biopsy. **July 2012** – Three new studies combined results for stereotactic and ultrasound guided CNB, so rate not calculable.	**December 2011 -** No new data. **July 2012** – No new data.	**December 2011 -** All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011 -** Conclusion still valid. **July 2012 -** Conclusion still valid.	**Up-to-date**	**Up-to-date**
It was not possible to calculate the ADH underestimation rate for ultrasound-guided vacuum-assisted core-needle biopsy. Strength of evidence: Insufficient	**December 2011 -** The only new studies reporting ADH underestimation rate combined results for ultrasound and stereotactically guided biopsy. **July 2012** – Three new studies combined results for stereotactic and ultrasound guided CNB, so rate not calculable.	**December 2011 -** No new data. **July 2012** – No new data.	**December 2011 -** All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011 -** Conclusion still valid. **July 2012 -** Conclusion still valid.	**Up-to-date**	**Up-to-date**
Ultrasound-guided automated gun core-needle biopsies have a sensitivity of 97.7 percent (95-percent CI: 97.2 to 98.2 percent). Strength of evidence: Low	**December 2011 -** No new studies. **July 2012** – Three new studies combined results for stereotactic and ultrasound guided CNB, so rate not calculable.	**December 2011 -** No new data. **July 2012** – No new data.	**December 2011 -** All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011 -** Conclusion still valid. **July 2012 -** Conclusion still valid.	**Up-to-date**	**Up-to-date**
Ultrasound-guided automated gun core-needle biopsies have a DCIS underestimation rate of 35.5% (95-	**December 2011 -** No new studies. **July 2012** – Three new studies combined results for stereotactic and ultrasound guided CNB, so rate not calculable.	**December 2011 -** No new data **July 2012** – No new data.	**December 2011 -** All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still	**December 2011 -** Conclusion still valid. **July 2012 -** Conclusion still valid.	**Up-to-date**	**Up-to-date**

Conclusions From CER	RAND Literature Search	FDA	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC	Conclusions of validity of CER conclusion(s)	
					Prior Assessment	Cumulative Assessment
percent CI: 27.1 to 45.0 percent). Strength of evidence: Low			valid.			
Ultrasound-guided automated gun core-needle biopsies have a 29.2 percent (95-percent CI: 23.4 to 35.9 percent). Strength of evidence: Low	**December 2011 -** No new studies. **July 2012** – Three new studies combined results for stereotactic and ultrasound guided CNB, so rate not calculable.	**December 2011 -** No new data. **July 2012** – No new data.	**December 2011 -** All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011 -** Conclusion still valid. **July 2012 -** Conclusion still valid.	**Up-to-date**	**Up-to-date**
Freehand automated gun core-needle biopsies have a sensitivity of 85.8 percent (95-percent CI: 75.8 to 92.1 percent). Strength of evidence: Low	**December 2011 -** Wei (2011) reported on 1,431 breast biopsies in China. The vast majority (91.5%) were freehand; sensitivity was 88.0%. Ward (2010) reported on 52 biopsies in the UK; 69.0% of classifications were upgraded upon repeat biopsy guided by ultrasound. **July 2012** – No new studies on freehand automated gun CNB	**December 2011 -** No new data. **July 2012** – No new data.	**December 2011 -** All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011 -** Conclusion is possibly out of date and this portion of the CER may need updating. However, as freehand biopsies are now rarely performed in the U.S. this should not be a priority. **July 2012 –** Same as above.	**Up-to-date**	**Up-to-date**
It was not possible to calculate the DCIS underestimation rate for freehand automated gun core-needle biopsies.	**December 2011 -** Wei, 2011 reported on 1,431 breast biopsies in China. The vast majority (91.5%) were freehand; DCIS underestimation rate was 36.2%. **July 2012** – No new studies on freehand automated gun CNB.	**December 2011 -** No new data. **July 2012** – No new data.	**December 2011 -** All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011 -** Conclusion is possibly out of date and this portion of the CER may need updating. However, as freehand biopsies are now rarely performed, this should not be a priority. **July 2012 –** Same as above.	**Up-to-date**	**Up-to-date**
It was not possible to calculate the	**December 2011 -** Wei (2011) reported on 1,431	**December 2011 -** No	**December 2011 -** All five experts agreed	**December 2011 -** Conclusion is possibly out of	**Up-to-date**	**Up-to-date**

Conclusions From CER	RAND Literature Search	FDA	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC	Conclusions of validity of CER conclusion(s)	
					Prior Assessment	Cumulative Assessment
ADH underestimation rate for freehand automated gun core-needle biopsies.	breast biopsies in China. The vast majority (91.5%) were freehand; ADH underestimate rate was 90.0% **July 2012** – No new studies on freehand automated gun CNB.	new data. **July 2012** – No new data.	conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	date and this portion of the CER may need updating. However, as freehand biopsies are now rarely performed, this should not be a priority. **July 2012 –** Same as above.		
There was insufficient evidence to estimate the accuracy of MRI-guided core-needle biopsies.	**December 2011** - No new studies on MRI guided CNB reported overall sensitivity rate. However, three studies reported cancellation rates to due to inadequate visualization; rate was 12.0% in Liberman, 2005, 13.0% in Han, 2008, and 8.0% in Brennan, 2011. Two studies reported DCIS underestimation rate: Liberman, 2005 (11.1%) and Malhaire, 2010 (25.0%). Regarding ADH underestimation, Liberman reported a rate of 50.0% and Malhiare reported a rate of 13.0%. Crystal, 2010, also reported an ADH underestimation rate of 50.0%. **July 2012** – Rauch, 2011, reported a 12% upgrade rate in 85 high risk lesions. Heller, 2012, reported upgrade rates from 13% to 57% in a systematic review which focuses primarily on accuracy of diagnosis by MRI, rather than by MRI guided CNB.	**December 2011** - No new data. **July 2012** – No new data.	**December 2011** - Four experts felt this conclusion was out of date. **July 2012** – One of the two experts reiterated this was out of date and suggested a reference.	**December 2011** - Conclusion is out of date. **July 2012** – Same as above.	**Out –of- date.**	**Out -of -date.**

Conclusions From CER	RAND Literature Search	FDA	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC	Conclusions of validity of CER conclusion(s)	
					Prior Assessment	**Cumulative Assessment**
Key Question 2. In women with a palpable for nonpalpable breast abnormality, what are the harms associated with different types of core-needle breast biopsy compared with open biopsy for diagnosis						
Severe complications following core-needle biopsy of any type are very rare, affecting fewer than 1 percent of procedures. Vacuum-assisted procedures may be associated with slightly more severe bleeding events than automated gun core-needle biopsies. Core-needle biopsies have a lower risk of complications than open surgical procedures.	**December 2011** - We found one new study of ultrasound guided vacuum assisted CNB that reported AEs. With 11 gauge needle, the rates for 136 "atypical" lesions were 8.8% hematoma, 5.1% venous bleeding, and 1.5% clip malposition. We found two new studies of MRI guided vacuum assisted CNB that reported AEs. In a French study of 72 lesions, there was one vasovagal reaction and one infection that was easily treated with antibiotics. In one US study of 95 lesions, there were 3 hematomas and one vasovagal reaction. **July 2012** – No new studies reported on AEs.	**December 2011** - No new data. **July 2012** – No new data.	**December 2011** - Four experts felt this conclusion was still valid. One expert felt there is underreporting for radiologically guided biopsies. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011** - Conclusion is out of date specifically for MRI guided CNB. **July 2012 –** Same as above.	**Our of-date**	**Out of-date**
Use of image guidance and vacuum assistance improved the accuracy of core-needle biopsy; however, vacuum assistance increased the percentage of procedures complicated by severe bleeding and hematoma formation.	**December 2011** - No new comparison data. **July 2012** – No new studies reported on AEs.	**December 2011** - No new data. **July 2012** – No new data.	**December 2011** - All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011** - Conclusion still valid. **July 2012 - -** Conclusion still valid.	**Up-to-date**	**Up-to-date**

Conclusions From CER	RAND Literature Search	FDA	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC	Conclusions of validity of CER conclusion(s)	
					Prior Assessment	Cumulative Assessment
Performing biopsies with patients seated upright increased the incidence of vasovagal reactions.	**December 2011** - No new studies. **July 2012** – No new studies reported on AEs.	**December 2011** - No new data.	**December 2011** - All five experts agreed conclusion still valid. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011** - Conclusion still valid. **July 2012 -** Conclusion still valid	**Up-to-date**	**Up-to-date**
Meta-regressions did not identify a statistically significant effect of the following factors on the accuracy or harms: needle size, method of verification of biopsy (open surgery, open surgery and at least 6 months' follow-up, or open surgery and at least 2 years' follow-up), whether the studies were conducted at a single center or at multiple centers, whether the studies were conducted in general hospitals or dedicated cancer clinics, or the country in which the study was conducted. Studies reported insufficient information about lesion	**December 2011** - As several new studies on accuracy were identified (results presented in question one above) a new meta-analysis could be conducted. Brennan (2011) conducted a meta-analysis of 52 studies including 7,350 lesions and found needle size (14 gauge vs 11 gauge), lesion size > 20mm, and palpability associated with misclassification. **July 2012** – One new study found misclassification associated with masses with irregular or speculated borders (as opposed to smooth.) Another new study found upgrade associated with non-circumscribed (as opposed to circumscribed) hypohecoic masses.	**December 2011** - No new data. **July 2012** – No new data.	**December 2011** - Four experts felt this conclusion was still valid. One expert felt this conclusion was out of date. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011** - Conclusion is possibly out of date and this portion of the CER may need updating. **July 2012 -** Conclusion still valid.	**Possibly out- of --date**	**Possibly out- of- date**

Conclusions From CER	RAND Literature Search	FDA	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC	Conclusions of validity of CER conclusion(s)	
					Prior Assessment	**Cumulative Assessment**
characteristics, patient characteristics, or the training or experience of the persons performing the biopsies to explore the effect of such factors on the accuracy or harms.						
Key Question 3: How do open biopsy and various core-needle techniques differ in terms of patient preference, availability, costs, availability of qualified pathologist interpretations, and other factors that may influence choice of a particular technique?						
There were no formal evidence-based conclusions. There was general agreement from experts that core-needle biopsy costs less than open surgical biopsy, consumes fewer resources and is preferred by patients. Women were generally satisfied with the cosmetic results of core-needle procedures.	**December 2011** - We found two studies that reported costs. In Italy, Abbate (2009) found the mean cost of ultrasound guided 11 gauge vacuum assisted CNB was 645 Euros versus 1,339 Euros for surgical biopsy. In contrast, in the US, Wolf (2008) found the mean cost of stereotactic or ultrasound guided 11 or 14 gauge CNB was $10,500 vs $11,500 for surgical biopsy; difference was not statistically significant. **July 2012** – No new studies reported cost.	**December 2011** - No new data. **July 2012** – No new data.	**December 2011** - Four experts felt this conclusion was still valid. One felt that the conclusion might differ for women age 60 and over. **July 2012** – Two experts responded; they agreed conclusion is still valid.	**December 2011** - Conclusion still valid. **July 2012 -** Conclusion still valid.	**Up-to-date**	**Up-to-date**
Women who underwent a core-needle biopsy as their first invasive test to diagnose a breast cancer had, on average, fewer surgical procedures	**December 2011** - No new studies. **July 2012** – No new studies.	**December 2011** - No new data. **July 2012** – No new data.	**December 2011** - Three experts felt this conclusion was still valid. One expert felt this is only true for women who have a benign diagnosis. One expert felt that	**December 2011** - Conclusion is possibly out of date (based on expert opinion) and this portion of the CER may need updating. **July 2012- Conclusion possibly out of date.**	**Possibly out- of -date**	**Possibly out –of- date**

Conclusions From CER	RAND Literature Search	FDA	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC	Conclusions of validity of CER conclusion(s)	
					Prior Assessment	Cumulative Assessment
than women who underwent an open biopsy procedure as their first invasive test. Women diagnosed with breast cancer by core-needle biopsy were usually able to have their cancer treated with a single surgical procedure, but women diagnosed with breast cancer by open surgical biopsy often required more than one surgical procedure to treat their cancer (odds ratio 13.7, 95-percent CI: 5.6 to 34.6). Strength of evidence: Moderate			evidence for fewer repeat surgeries following core biopsy is lacking. **July 2012** – Two experts responded; they agreed conclusion is still valid.			

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Appendices

Appendix A. Search Strategy

DATABASE SEARCHED & TIME PERIOD COVERED:
Medline on OVID – 2011-6/21/2012

LANGUAGE:
English

SEARCH STRATEGY:
breast.mp. OR exp breast cancer/di OR exp breast neoplasms/di OR exp breast disease/di OR exp breast diseases/di OR ((breast OR mammar$) AND (papilloma OR calcification$ OR calcinosis OR tum?or$ OR lesion$ OR cancer OR carcinoma$ OR lump$)).mp.
AND
biops$.mp.
AND
(large core OR large-core OR needle OR percutaneous OR mammotome OR mammatome OR vacuum).mp. OR su.fs. OR open.mp. OR excision$.mp. OR incision$.mp. OR surgical.mp. OR breast/su OR breast tumor/su

OR

(stereotactic breast biopsy OR directional vacuum assisted biopsy).mp.

NOT

(letter OR editorial OR news OR comment OR case reports OR note OR conference paper).de.

NUMBER OF RESULTS: 793
NUMBER AFTER REMOVAL OF DUPLICATES: 363

FILTERED TO INCLUDE ONLY THE FOLLOWING JOURNALS:
Annals of Internal Medicine
British Medical Journal
JAMA
Lancet
New England Journal of Medicine

American Journal of Roentgenology
Breast
Breast Journal
Pathology
Radiology

NUMBER OF RESULTS FROM THESE JOURNALS: 32

Appendix B. Comparative Effectiveness of Core Needle Biopsy and Open Surgical Biopsy for Diagnosis of Breast Lesions, July 2012 re-assessment

Author, Year	Country	Type of Biopsy	Lesions	Accuracy results	Harms	Impact of factors (patient, tumor, provider)	Patient preference, cost, availability
STEREOTACTIC GUIDED							
Bianchi, 2011[17]	Italy	11 gauge stereotactic vacuum assisted CNB	1,644 "borderline" B3 lesions	21.1% positive predictive rate, for AEPDT 27.3% positive predictive rate	ND	ND	ND
Eby, 2009[2]	UK	9 or 11 gauge stereotactic vacuum assisted CNB	141	ADH underestimation rate 21.6% for 9 gauge, 20.4% for 11 gauge	ND	ND	ND
Kohr, 2010[15]	US	9 or 11 gauge stereotactic vacuum assisted CNB	101 atypical ductal hyperplasia (ADH)	ADH underestimation rate 19.8%	ND	Underestimation associated with 3 or more foci of ADH	ND
Salem, 2009[14]	France	10 gauge stereotactic vacuum assisted CNB	58	ADH underestimation rate 18.2%, DCIS underestimation rate 19.2%	ND	ND	ND
Teng-Swan Ho, 2008[11]	Singapore	11 gauge stereotactic vacuum assisted CNB	61 ADH	DCIS underestimation rate 23%	ND	No association of underestimation with morphology of calcifications, negative predictive value associated with powdery or amorphous calcifications	ND
Wiratkapun, 2010[5]	Thailand	11 gauge stereotactic vacuum assisted CNB	64	Sensitivity 95.5%, ADH underestimation rate 50%, no DCIS underestimation, false negative rate 4.5%	ND	ND	ND
ULTRASOUND GUIDED							

Author, Year	Country	Type of Biopsy	Lesions	Accuracy results	Harms	Impact of factors (patient, tumor, provider)	Patient preference, cost, availability
Abbate, 2009[13]	Italy	11 gauge ultrasound guided vacuum assisted CNB	136 C3 (atypical, probably benign) lesions	Sensitivity 94.8%, specificity 100%,	8.8% hematoma, 5.1% venous bleeding, 1.5% clip malposition	ND	Mean cost 645 Euros versus 1,339 Euros for surgical biopsy
MRI GUIDED							
Brennan, 2011--Cancelation of[19]--	US	MRI guided CNB	911	ND	8.0% of these biopsies cancelled due to non-visualization	ND	ND
Crystal, 2011[9]	Canada	9 gauge MRI guided vacuum assisted CNB	26 high risk	ADH underestimation rate 50.0%, total underestimation 50.0%		No association of underestimation with morphology	ND
Han, 2008[7]	US	various gauges, MRI guided vacuum assisted CNB	150	Inadequate rate of surgical biopsy comparison or 6 month f/u	13% of biopsies cancelled due to nonvisualization /decreased visualization	ND	ND
Heller, 2012[23] SYSTEMATIC REVIEW	**U.S.**	**MRI guided vacuum assisted CNB, various gauges**	**High risk lesions - various**	**No new studies to include. Upgrade rate ranged from 13% to 57%. Review focused primarily on accuracy of diagnosis by breast MRI, rather than MRI guided CNB**	**ND**	**ND**	**ND**
Liberman, 2005[8]	US	9 gauge MRI guided vacuum assisted CNB	95	DCIS underestimation rate 11.1%, ADH underestimation rate 50.0%	12% of biopsies cancelled due to nonvisualization. Biopsy AEs: 3 hematomas, one vasovagal reaction	Median time 33 minutes per lesion	ND
Malhaire,	France	10 gauge MRI	72	DCIS underestimation rate	Aes - One	Underestimation associated	72 minutes

Author, Year	Country	Type of Biopsy	Lesions	Accuracy results	Harms	Impact of factors (patient, tumor, provider)	Patient preference, cost, availability
2010[10]		guided vacuum assisted CNB		25.0%, ADH underestimation rate 13.0%	vasovagal reaction, one infection treated with antibiotics	with less experienced MDs	mean time per procedure
Rauch, 2012[25]	**U.S.**	**9 gauge MRI-guided vacuum-assisted CNB**	**85 high risk lesions**	**12% upgrade rate**	**ND**	**Probability of malignancy significantly high in masses with iregrular or speculated borders than in smooth masses.**	**ND**
FREEHAND							
Ward, 2010[16]	UK	14 gauge freehand CNB	52	69.0% of classifications upgraded upon repeat biopsy guided by ultrasound	ND	Misclassification associated with depth, size	ND
Wei, 2011[4]	China	14 or 16 gauge freehand or ultrasound guided CNB	1,431	Sensitivity 88.0%, ADH underestimation rate 90.0%, DCIS underestimation rate 36.2%	ND	Vast majority (91.5%) were freehand; no breakdown of results by whether guided	ND
MIXED GUIDANCE							
Bianchi, 2012[17]	**Italy**	**14 gauge ultrasound or stereotactic guided CNB**	**49 diagnosed as radial scar (RS) without associated atypical epithelial proliferation**	**8.2% underestimation rate**	**ND**	**All upgraded cases were originally diagnosed as non circumscribed hypohecoic mass, while no cases of circumscribed hypohecoic masses were upgraded.**	**ND**
Brennan, 2011--Ductal Carcinoma[18]	US	11 or 14 gauge CNB - assorted	7,350	Meta-analysis of 52 studies: DCIS underestimation rate 23.9%	ND	14 gauge (vs 11 gauge), lesion size > 20mm, palpability, associated with misclassification	ND

Author, Year	Country	Type of Biopsy	Lesions	Accuracy results	Harms	Impact of factors (patient, tumor, provider)	Patient preference, cost, availability
Destounis, 2012[22]	**U.S.**	**Stereotactic, ultrasound, or MRI guided CNB, various gauges**	**64 diagnosed as LCIS**	**33.3% underestimation rate, no data by guidance type**	**ND**	**Inadequate power to detect significance of tumor type**	**ND**
Ibrahim, 2012[24]	**Canada**	**14 gauge ultrasound guided, 11 gauge stereotactic vacuum-assisted, or 14 gauge stereotactic guided CNB**	**126 diagnosed as LCIS and/or ALH**	**34% underestimation rate, difference by guidance or needle type not statisically significant**	**ND**	**40% of LCIS diagnoses upgraded, 27% of ALH diagnoses upgraded - difference not statisically significant**	**ND**
Londero, 2011[6]	Italy	14 gauge ultrasound guided CNB or 11 gauge stereotactic vacuum assisted CNB	300 borderline (B3)	Ultrasound guided automatic gun CNB: ADH under estimation rate 33%, total malignancy underestimation 12.7% Stereotactic vacuum assisted CNB: ADH underestimation 22%, total malignancy underestimation 12.5%	ND	ND	ND
Richter-Ehrenstein, 2011[20]	Germany	14 gauge ultrasound guided CNB or 11 gauge stereotactic vacuum assisted CNB	61 diagnosed as intraductal papilloma	DCIS underestimation rate 25%	ND	ND	ND
Wolf, 2008[12]	US	11 or 14 gauge stereotactic or ultrasound guided CNB	108 BIRADS = 5	Sensitivity 93.0%	ND	ND	Total charges $10,500 for CNB, vs $11,500 for

Author, Year	Country	Type of Biopsy	Lesions	Accuracy results	Harms	Impact of factors (patient, tumor, provider)	Patient preference, cost, availability
							surgical biopsy (NS)
Yu, 2010[3]	assorted	8, 10, 11 or 14 gauge stereotactic or ultrasound guided vacuum assisted CNB	21 studies, 5,535 patients	Sensitivity 98.1%, specificity 99.9%, ADH underestimation rate 20.9% in 9 studies, DCIS underestimation rate 11.2% in 12 studies	ND	Type of guide, size of gauge not associated with accuracy	ND

Bold = new studies from the July 2012 re-assessment

Legend: ADH-Atypical Ductal Hyperplasia; AEPDT-Atypical Epithelial Proliferation of Ductal Type; CNB-Core-Needle Biopsy; DCIS-Ductal Carcinoma In Situ; LCIS-Lobular Carcinoma In Situ; ND-Not described; MRI-Magnetic Resonance

Appendix C. Questionnaire Matrix

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
Key Question 1: In women with a palpable or nonpalpable breast abnormality, what is the accuracy of different types of core-needle breast biopsy compared with open biopsy for diagnosis?			
Stereotactically guided vacuum-assisted core-needle biopsies have a sensitivity of 99.2 percent (95-percent confidence interval [CI]: 97.9 to 99.7 percent). Strength of evidence: Low	☐	New Evidence: _____ _____ _____	☐
Stereotactically guided automated gun core-needle biopsies have a sensitivity of 97.8 percent (95-percent CI: 95.8 to 98.9 percent). Strength of evidence: Low	☐	New Evidence: _____ _____ _____	☐
Ultrasound-guided vacuum-assisted core-needle biopsies have a sensitivity of 96.5 percent (95-percent CI: 81.2 to 99.4 percent). Strength of evidence: Low	☐	New Evidence: _____ _____	☐

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
Ultrasound-guided automated gun core-needle biopsies have a sensitivity of 97.7 percent (95-percent CI: 97.2 to 98.2 percent). Strength of evidence: Low	☐	New Evidence: _____ _____ _____	☐
Freehand automated gun core-needle biopsies have a sensitivity of 85.8 percent (95-percent CI: 75.8 to 92.1 percent). Strength of evidence: Low	☐	New Evidence: _____ _____ _____	☐
There was insufficient evidence to estimate the accuracy of MRI-guided core-needle biopsies	☐	New Evidence: _____ _____ _____	☐
Key Question 2. In women with a palpable for nonpalpable breast abnormality, what are the harms associated with different types of core-needle breast biopsy compared with open biopsy for diagnosis			

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
Severe complications following core-needle biopsy of any type are very rare, affecting fewer than 1 percent of procedures. Vacuum-assisted procedures may be associated with slightly more severe bleeding events than automated gun core-needle biopsies. Core-needle biopsies have a lower risk of complications than open surgical procedures.	☐	New Evidence: _____ _____ _____	☐
Use of image guidance and vacuum assistance improved the accuracy of core-needle biopsy; however, vacuum assistance increased the percentage of procedures complicated by severe bleeding and hematoma formation.	☐	New Evidence: _____ _____ _____	☐
Performing biopsies with patients seated upright increased the incidence of vasovagal reactions.	☐	New Evidence: _____ _____ _____	☐

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
Meta-regressions did not identify a statistically significant effect of the following factors on the accuracy or harms: needle size, method of verification of biopsy (open surgery, open surgery and at least 6 months' follow-up, or open surgery and at least 2 years' follow-up), whether the studies were conducted at a single center or at multiple centers, whether the studies were conducted in general hospitals or dedicated cancer clinics, or the country in which the study was conducted. Studies reported insufficient information about lesion characteristics, patient characteristics, or the training or experience of the persons performing the biopsies to explore the effect of such factors on the accuracy or harms.		_____ _____ _____	
Key Question 3: How do open biopsy and various core-needle techniques differ in terms of patient preference, availability, costs, availability of qualified pathologist interpretations, and other factors that may influence choice of a particular technique?			
There were no formal evidence-based conclusions. There was general agreement from experts that core-needle biopsy costs less than open surgical biopsy, consumes fewer resources and is preferred by patients. Women were generally satisfied with the cosmetic results of core-needle procedures.	☐	New Evidence: _____ _____ _____	☐

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
Women who underwent a core-needle biopsy as their first invasive test to diagnose a breast cancer had, on average, fewer surgical procedures than women who underwent an open biopsy procedure as their first invasive test. Women diagnosed with breast cancer by core-needle biopsy were usually able to have their cancer treated with a single surgical procedure, but women diagnosed with breast cancer by open surgical biopsy often required more than one surgical procedure to treat their cancer (odds ratio 13.7, 95-percent CI: 5.6 to 34.6). Strength of evidence: Moderate		New Evidence: _____ _____ _____ _____	
Are there new data that could inform the key questions that might not be addressed in the conclusions?			