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#### **Ultrasound in the Diagnosis & Management of Pleural Effusions**

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#### Abstract

We review the literature on the use of point-of-care ultrasound to evaluate and manage pleural effusions. Point-of-care ultrasound is more sensitive than physical exam and chest radiography to detect and characterize pleural fluid, and avoids many negative aspects of computerized tomography (CT). Additionally, point-of-care ultrasound can be used to assess pleural fluid volume and character, revealing possible underlying pathologies and guiding management. Thoracentesis performed with ultrasound guidance has lower risk of pneumothorax and bleeding complications. Future research should focus on the clinical-effectiveness of point-of-care ultrasound in the routine management of pleural effusions and how new technologies may expand its clinical utility.

Hospitalists commonly encounter pleural effusions, and their detection and characterization by point-of-care ultrasound can guide management. Approximately 44–57% of hospitalized patients with bacterial pneumonia<sup>1,2</sup> and up to 62% of ICU patients<sup>3</sup> have a pleural effusion. For patients with parapneumonic effusions, hospitalists can use ultrasound to quantify and characterize pleural fluid to determine whether diagnostic or therapeutic drainage is indicated, as well as to guide performance of thoracentesis. For patients with lung cancer, detection of a malignant pleural effusion changes staging to stage IV, regardless of tumor size or lymph node involvement, and hospitalists may discuss more appropriate treatment options with patients and consultants.

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Routine use of pleural ultrasonography may help hospitalists provide high value care by reducing ancillary testing, including CT scans that expose patients to ionizing radiation, and reducing complications of thoracentesis. However, many hospitalists may not be familiar with use of point-of-care ultrasound. A national survey in 2012 revealed only 25% of internal medicine residencies have formal curricula to teach point-of-care ultrasonography.<sup>4</sup> The purpose of this review is to provide an overview of how point-of-care ultrasound can be utilized by hospitalists in the care of patients with pleural effusions. We review the literature on the diagnosis and evaluation of pleural effusions with ultrasound, as well as techniques to examine and drain the pleural space.

#### **Diagnosis of Pleural Effusion**

#### History & Physical Exam

Pleural effusions are most commonly associated with heart failure, pneumonia, cancer, pulmonary embolism, viral disease, coronary artery bypass surgery, and cirrhosis with ascites. The most common symptoms related to pleural effusion are non-specific and often indistinguishable from those of the underlying disease process, including cough, dyspnea, and pleuritic chest pain.<sup>5</sup>

Diagnostic accuracy of physical examination to detect pleural fluid is highly dependent on the size of the effusion and is unlikely to detect effusions <300ml. A systematic review found the most accurate physical exam findings to rule in a pleural effusion were dullness to percussion (positive likelihood ratio [LR] of 8.7; 95% CI, 2.2–33) and asymmetric chest expansion (positive LR of 8.1; 95% CI, 5.2–12.7). Normal tactile vocal fremitus was the most accurate physical exam finding to rule out a pleural effusion (negative LR, 0.21; 95% CI, 0.12–0.37).<sup>6</sup> A major limitation of all these studies is that physical exam was compared to chest radiography as the reference standard, and posterior-anterior chest radiographs are not sensitive for detection of pleural effusions until 200mL of fluid has accumulated.<sup>7</sup> Further, chest percussion penetrates to a maximum depth of 6cm, limiting its utility in obese patients.<sup>8</sup> Characteristics of pleural fluid that often change management, such as loculations, cannot be detected by physical exam.

#### Chest Radiography

Chest radiography has traditionally been used to diagnose pleural effusions. Free-flowing pleural fluid collects in the most dependent portions of the thorax, initially in the subpulmonic space followed by the costophrenic recesses. Pleural fluid is detectable in the costophrenic recesses on lateral upright chest radiograph after 50mL has accumulated. On standard posterior-anterior chest radiograph, blunting of the costophrenic recesses and obliteration of the hemidiaphragm are seen when >200mL and >500mL of pleural fluid have accumulated, respectively.<sup>7</sup> However, upright chest radiographs can miss a considerable number of effusions, including as many as 10% of parapneumonic effusions large enough to indicate need for drainage.<sup>9</sup> Supine anterior-posterior chest radiographs can miss a significant proportion of large effusions seen on chest CT, <sup>10</sup> ultrasound, <sup>11</sup> and lateral decubitus radiographs.<sup>12</sup> Pleural effusions are frequently mistaken for parenchymal opacities on portable anterior-posterior chest radiographs.<sup>10</sup>

#### **Computerized Tomography**

Chest CT serves as the reference standard in most modern diagnostic accuracy studies. Limitations of chest CT include difficulty distinguishing small effusions from pleural thickening, dependent atelectasis, or tumor; lower sensitivity for detecting pleural fluid septations compared to ultrasound;<sup>13</sup> exposure of patients to approximately 7mSv of ionizing radiation, the equivalent radiation dose of 350 chest radiographs;<sup>14</sup> high cost; and need to transport patients to radiology departments where CT scanners are located.

#### Pleural Ultrasonography

Ultrasound can rapidly differentiate conditions that demonstrate a non-specific, radiopaque appearance of lower lung fields on chest radiographs, including pleural effusions, pneumonia, atelectasis, elevated hemi-diaphragm, and lung or pleural masses. Advantages of point-of-care ultrasound include the ability of hospitalists to acquire and interpret images at the bedside, and integrate findings into clinical decision-making immediately. Multiple studies have demonstrated superior diagnostic accuracy of ultrasound compared to chest radiography for detection of pleural effusions. Pleural ultrasound can detect physiologic amounts of pleural fluid (5ml),<sup>15</sup> but a minimal volume of 20ml is more reliably detected,<sup>16</sup> and ultrasound is 100% sensitive for effusions >100ml.<sup>17</sup> In a prospective study of critically ill patients with ARDS, the diagnostic accuracy of ultrasound for pleural effusions was superior (93%), compared to auscultation (61%) and anterior-posterior chest radiograph (47%), using chest CT as the reference standard.<sup>18</sup> A meta-analysis of four studies calculated a pooled sensitivity and specificity of ultrasound for detection pleural effusions as 93% (95% CI, 89% to 96%) and 96% (95% CI, 95% to 98%), respectively.<sup>18-22</sup> Ultrasound has the additional benefit of characterizing underlying lung parenchyma which is well described in the literature but beyond the scope of this review.<sup>23</sup>

Sensitivity and specificity of chest radiography and ultrasonography to detect a pleural effusion are displayed in Table 1.<sup>9–12,18,20–22,24–26</sup>

#### **Pleural Ultrasound Examination**

A pleural ultrasound exam may be performed as part of a complete lung ultrasound exam, such as the BLUE protocol,<sup>27</sup> or a focused exam to evaluate a suspected or known pleural effusion seen on chest radiograph or CT scan.<sup>27</sup> Free-flowing pleural effusions accumulate in the most dependent portions of the thorax – most commonly, the posterolateral costophrenic recesses in semi-recumbent or seated patients, but anteriorly in mechanically ventilated patients in prone position.

A low-frequency (2–5 MHz) phased-array transducer is generally preferred for imaging in between the ribs. High-frequency linear transducers do not provide adequate penetration to visualize deep structures, but do provide superior visualization of the pleural line to assess pleural thickness, measure pleural depth, and evaluate for pneumothorax.

Pleural effusions are best evaluated starting at the level of the diaphragm. Place the transducer in a longitudinal plane on the posterior axillary line at the level of the diaphragm with the transducer orientation marker ("notch") pointed cephalad (Figure 1). Five structures

must be definitively identified to diagnose a pleural effusion: liver/spleen, diaphragm, pleural fluid, lung, and chest wall (Figure 2A). Large pleural effusions compress adjacent lung causing atelectasis, which gives the lung a tissue-like echogenicity similar to the liver (Figure 2B). Static air bronchograms are commonly seen in atelectatic lung bases with pleural effusions.<sup>28</sup>

Color flow Doppler and M-mode ultrasound may be utilized as adjuncts to routine 2dimensional ultrasonography. Free-flowing pleural effusions will demonstrate flow by color Doppler (Figure 3A). Using M-mode ultrasound, lung can been seen moving within a pleural effusion to and from the chest wall ("sinusoid sign").<sup>29</sup> Absence of flow or movement is seen with dense pleural loculations, pleural thickening, and peripheral lung or pleural masses (Figure 3B).

#### **Characterization of Pleural Effusion**

#### Pleural Fluid Volume

Quantification of pleural fluid volume has been proposed using formulas with sonographic measurements.<sup>30–32</sup> These formulas are most accurate for moderate-sized effusions but have not been validated beyond individual study cohorts. The largest study (n=150) found a strong correlation between calculated and actual volumes drained by thoracentesis ( $r^2$ =0.79; p<0.001) using the formula [Volume (mL) = 16×parietal to visceral pleura distance (mm) at the mid-diaphragm].<sup>31</sup> Although an accurate quantitative pleural fluid volume assessment may be possible, these formulas are not commonly used in clinical practice. A qualitative assessment is adequate for most clinical decision-making using categories of minimal, small, moderate, or large volume.

#### Simple vs. Complex Effusions

Based on its sonographic appearance, pleural effusions are categorized as simple or complex. Simple pleural effusions are anechoic, and usually transudative. Complex pleural effusions are subcategorized as homogeneously or heterogeneously echogenic, with or without septations, and are more often exudative.<sup>33</sup>

Effusions with heterogeneous echogenicity with swirling echoes suggest high cellular content that is often associated with malignancy.<sup>34</sup> Fibrinous stranding, septations, and loculations also suggest an exudative effusion (Figure 4A), and are more readily identified and characterized on lung ultrasound than CT scan.<sup>35</sup>

Homogenously echogenic effusions are most often due to hemothorax or empyema.<sup>36</sup> The high cell count of a hemothorax creates a layering effect in costophrenic recesses ("hematocrit sign"). Empyemas develop from complex effusions that organize into collections of pus and usually have a homogeneously echogenic, speckled appearance (Figure 4B). Sonographic evidence of septations in the presence of empyema predicts the need for intrapleural fibrinolytic therapy, longer duration of drainage, and possible surgical intervention.<sup>37</sup>

Isolated dense loculations may be challenging to differentiate from peripheral lung or pleural lesions, such as abscess or tumor. Solid pleural and peripheral lung lesions are generally hypoechoic and demonstrate absence of flow by color Doppler ultrasound.

#### **Pleural Thickness**

Normal visceral and parietal pleura are apposed and 0.2–0.3mm thick.<sup>38</sup> Pleural effusions with parietal pleural thickness >10mm, pleural nodularity, and diaphragmatic thickness >7 mm predicted underlying malignancy with high specificity and positive predictive value in one study.<sup>39</sup> As many as 20% of anechoic lesions of the pleura are solid rather than fluid. Color flow Doppler ultrasound can differentiate small pleural effusions from solid pleural abnormalities with sensitivity and specificity of 89% and 100%, respectively.<sup>40</sup>

#### Pleural Fluid Drainage

Since its first description in 1967, use of ultrasound guidance for thoracentesis has evolved to become the standard-of-care in many hospitals in the United States.<sup>41</sup> The British Thoracic Society (BTS) guidelines recommend that all thoracenteses be performed with ultrasound guidance.<sup>42</sup> The American College of Graduate Medical Education (ACGME) now requires proficiency in use of ultrasound for thoracentesis and pleural catheter insertion by pulmonary and critical care fellows.<sup>43</sup>

The impetus for these recommendations stems from increased procedural success and decreased complications associated with ultrasound-guided drainage of pleural effusions. A study evaluating thoracentesis site selection based on physical exam and chest radiographs demonstrated inaccurate site selection in 15% of patients, and use of ultrasound for site selection prevented possible accidental organ puncture in 10% of all cases.<sup>44</sup> Success rate of thoracentesis for small pleural effusions has been shown to increase from 66% to 90% with ultrasound guidance.<sup>42</sup> Using ultrasound, the distance from the skin to parietal and visceral pleura can be measured to determine whether thoracentesis can be safely performed, and to guide selection of an adequate length needle (Figure 5). A minimum pleural effusion depth of 1.5cm between the visceral and parietal pleura has been recommended to perform diagnostic thoracentesis.<sup>28</sup> Diagnostic thoracentesis of complex septated pleural effusions or empyemas may be performed with a straight needle, but therapeutic drainage often requires temporary insertion of a catheter. Traditionally, large-bore chest tubes (> 24F) had been advocated to drain viscid pus, but recent evidence suggests that small-bore catheters (10-14F) with instillation of thrombolytics may be as effective and performed with less discomfort.<sup>45</sup> Video-assisted thoracoscopy to lyse septations and evacuate infected materials is indicated when chest tube drainage has failed.

The most common complication of pleural drainage is pneumothorax. A meta-analysis demonstrated a reduction in post-thoracentesis pneumothorax rates from 9% to 4% with use of ultrasound.<sup>46</sup> Transporting patients to radiology for ultrasound marking has not been shown to decrease pneumothorax rates compared to thoracentesis without ultrasound guidance, likely due to changes in patient position and prolonged delays between marking and drainage.<sup>47</sup> Post-procedure pneumothorax can be ruled out if lung sliding is visualized. A meta-analysis demonstrated superior sensitivity and similar specificity of pleural

ultrasonography versus chest radiography to detect pneumothorax (sensitivity 91% vs. 50% and specificity 98% vs. 99%, respectively).<sup>48</sup> Real-time ultrasound guidance for thoracentesis, or use of ultrasound to track the needle tip, has not been well studied but may be performed by experienced proceduralists to drain small effusions.

#### Future Research

Future research should focus on the clinical effectiveness of point-of-care pleural ultrasonography when integrated with other diagnostic tools and application of new ultrasound technologies to evaluate pleural diseases. Routine use of point-of-care ultrasound as the primary imaging modality in a medical intensive care unit demonstrated a highly statistically significant reduction in chest x-rays (3.75 vs. 0.82, P<0.0001) and chest CT scans (0.10 vs. 0.04, P=0.0007).<sup>49</sup> Similar studies have yet to be performed with the use of ultrasound in the management of pleural diseases. Thus, clinical effectiveness studies are needed to assess the impact of routine use of pleural ultrasound on the initiation of appropriate therapies, length of stay, and costs in the management of pleural effusions.

Point-of-care pleural ultrasound findings need to be evaluated in the context of other clinical findings and diagnostic tests. Certain ultrasound findings have been associated with exudative pleural effusions, but whether exudative and transudative effusions can be differentiated non-invasively using ultrasound findings alone, or in combination with other clinical data, warrants investigation. Similar to severity of illness scores, models that incorporate clinical, laboratory, and ultrasound findings need to be developed to guide treatment decisions, such as type of drainage procedure, as well as prognostication.

Finally, new technologies may advance the utility of point-of-care pleural ultrasonography. Even though 3-dimensional ultrasonography has been available for over two decades, comparative studies of conventional 2-dimensional versus 3-dimensional ultrasonography to characterize pleural effusions have yet to be performed. Further, computer-aided detection has been shown to facilitate interpretation of ultrasound images, but this technology has yet to be applied to pleural ultrasonography.

#### Conclusions

Point-of-care pleural ultrasound is a powerful bedside tool in the hospitalist's armamentarium that is superior to physical examination and chest radiographs in the detection and characterization of pleural effusions. Further, ultrasound performs similarly when compared to CT scans but offers the advantages of decreased cost, avoidance of ionizing radiation, and availability at the bedside. Ultrasound guidance reduces complications and increases the success rate of pleural drainage procedures, leading to improved patient safety. As clinical effectiveness studies emerge revealing its true value, point-of-care pleural ultrasonography is likely to become the standard diagnostic tool to evaluate and manage patients with pleural effusions.

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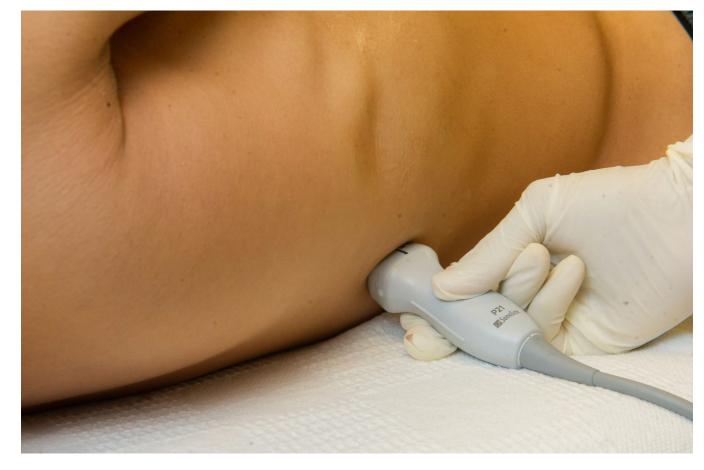
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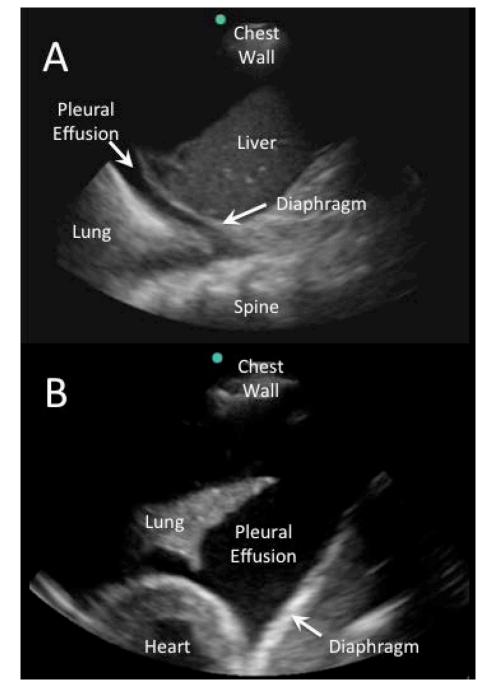
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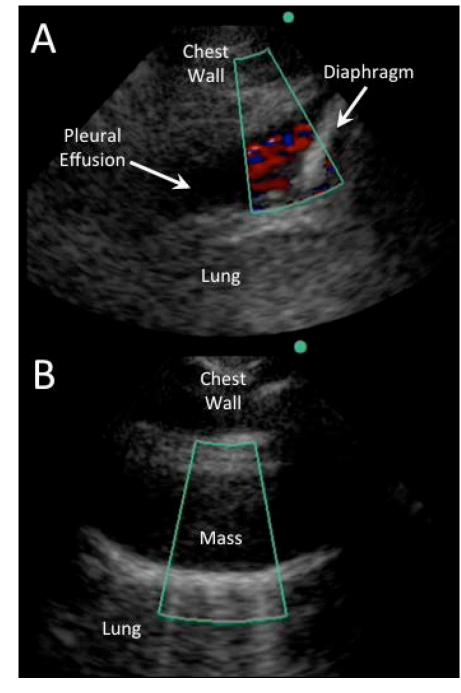
#### Figure 1.

Transducer position. In *supine or semi-recumbent* patients, the transducer is placed longitudinally on the posterior axillary line at the level of the diaphragm. The transducer should be wedged in between the patient and the bed to visualize the most dependent pleural space.



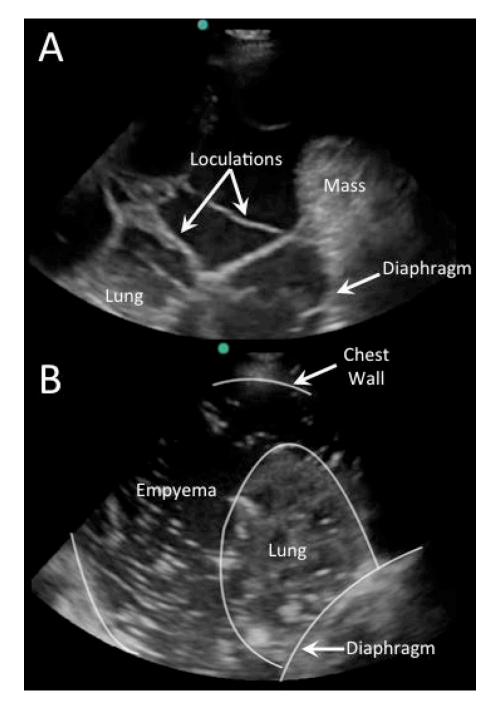
#### Figure 2.

A) Small pleural effusion (right chest). A small pleural effusion is shown with adjacent structures that should be definitively identified, including the liver, diaphragm, lung, and chest wall. B) Large pleural effusion (left chest). Large pleural effusions cause compressive atelectasis of adjacent lung, giving the lung a tissue-like echogenicity. Note the heart is often visualized in the far field with large left-sided pleural effusions.



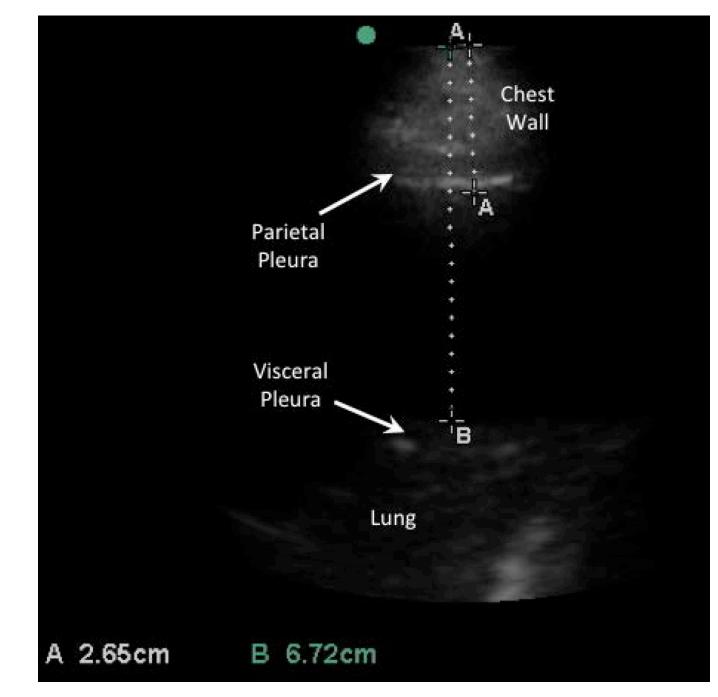
#### Figure 3.

A) Free-flowing pleural effusion. Color flow Doppler demonstrates movement of pleural fluid in the costophrenic recess with respiration. B) Pleural mass. Absence of flow by color Doppler is demonstrated with a hypoechoic pleural mass that could be mistaken for a pleural effusion.



#### Figure 4.

A) Loculated pleural effusion. A complex pleural effusion with loculations between the lung, diaphragm, and a diaphragmatic metastasis is demonstrated. B) Empyema. The echogenic, speckled appearance of a large empyema with underlying consolidated lung is shown in a transverse view.



#### Figure 5.

Measurement of pleural fluid depth. The distance between the skin and parietal and visceral pleura can be measured prior to thoracentesis to determine the minimum and maximum depths to safely insert a needle.

## Table 1

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nest radiography vs. ultrasonography for detect
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Chest radiograph

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Chest radiograph	Supine AP	Woodring <sup>24</sup>	Upright PA/Lateral	92%	
		Ruskin <sup>12</sup>	Lateral decubitus XR	67%	70%
		Emamian <sup>11</sup>	Ultrasound	82%	82%
		Kocijancic <sup>25</sup>	Ultrasound or thoracentesis	33%	
		Lichtenstein <sup>18</sup>	CT	39%	85%
		Kitazano <sup>10</sup>	CT	66%	89%
		Xirouchaki <sup>26</sup>	CT	65%	81%
		Brixey <sup>9</sup>	CT	78%	76%
	Lateral Decubitus	Kocijancic <sup>25</sup>	Ultrasound or thoracentesis	94%	100%
	Upright PA	Brixey <sup>9</sup>	CT	82%	81%
	Lateral Upright	Brixey <sup>9</sup>	CT	86%	88%
Ultrasound	Cardiology	Kataoka <sup>20</sup>	CT	93%	%88
	Point-of-care	$Ma^{21}$	CT or tube thoracostomy	%96	100%
		Lichtenstein <sup>18</sup>	CT	92%	93%
		Rocco <sup>22</sup>	CT	94%	%66
		Xirouchaki <sup>26</sup>	CT	100%	100%