

Intracardiac echocardiography for guiding biopsy of cardiac tumors: a novel noninvasive technique

Since intracardiac echocardiography (ICE) was introduced into clinical practice about 20 years ago, the application of ICE in cardiac procedure has gradually expanded. Currently, ICE is most prevalent in electrophysiologic procedures, percutaneous device closures and the emerging transcatheter aortic valve implantation technique. Considering the various advantages of ICE shown in other cardiac procedures, these could also be applied to biopsy for cardiac tumors. Although cardiac biopsy is not a common procedure, the prognosis of cardiac tumor presents critical variation according to the primary pathology, and tissue diagnosis is essential for the treatment plan. Therefore, we should improve the current quality of cardiac biopsy, and the novel imaging modality; ICE could be important for this aim.

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Because the cardiac tumors manifest with nonspecific clinical features, those are usually detected on cardiac imaging performed for other causes. However, owing to recent wide use of echocardiography and other imaging modalities, cardiac tumor is not very unusual in a real clinical practice. As the definite diagnoses of most tumors are made by pathologic confirmation, the golden standard for diagnosis and treatment is complete excision. However, it is unavailable for many reasons, and the cardiac biopsy is considered as alternative approach. According to the American Heart Association/American College of Cardiology/European Society of Cardiology (AHA/ACC/ESC) 2007 guidelines [1]; the cardiac biopsy is reasonable if the diagnosis cannot be established by noninvasive modality, and if the pathologic diagnosis influence the treatment plans. There is critical variation in prognosis among malignant primary cardiac tumors; the life expectancy of sarcoma is less than 1 year, whereas it could be up to 5 years in lymphoma [2]. Metastatic cardiac tumor

is much common as the previous autopsy series reported the prevalence of intracardiac metastasis to be above 10% [3]. In metastatic setting, occasionally the cardiac biopsy is useful; it helps to plan a systemic treatment and to avoid invasive biopsy for another site. Basically, cardiac biopsy is the intraluminal access, the potential risk of bleeding – in other words, extravasation – would be much reduced compared with the explorations for other sites.

However, there have been several technical challenges in the cardiac biopsy. First, the fluoroscopy is actually very limited in spatial information, but it only shows cardiac silhouette. Therefore, it is insufficient to ensure the precise location and depth in sample acquisition [4]. Second, as the target is constantly moving with heart beats, respiration and blood flow; the temporal resolution of image is another requirement [5]. Third, the wall thickness is variable (especially, 2–5 mm in left atrium [6]) that the operator should be cautious to perforation or laceration. Also the operator should be cautious to the neighboring struc-

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tures such as ascending aorta and lung. In this background, there has been a demand for a delicate imaging modality, and some operators use the echocardiography in combination with fluoroscopy [1]. This brief report is focused on intracardiac echocardiography (ICE) with overview for the basic concepts, technical advantages and current limitations. To the present, firm evidence about the application of ICE in cardiac biopsy is lacking; it has only been shown in several case reports, not in large-sized patient group. Therefore in this emerging field, it may be a practical way to review the lessons from other noncoronary procedures using ICE.

Overview of ICE

Usually, the ICE catheters access through femoral or jugular vein and the tips are placed in right atrium (RA) in which the navigation starts [7]. The operator can adjust the catheter for the position, orientation and angle to acquire the optimal images (Figure 1). The first commercially available system was the UltraICE® (Boston Scientific, MA, USA), a rotational catheter with a 9 MHz single element transducer [8,9]. It provides imaging sector of 360° with depth up to 5 cm [8,9]. This system is not steerable, and lacks of Doppler imaging [8,9]. The following models are the AcuNav® (Siemens-Acuson, Inc., CA, USA) and ViewFlex Plus® (St. Jude Medical, MN, USA) those are 64-element phased-array systems. The AcuNav has 5.0–10.0 MHz transducers, imaging sector of 90° with tissue penetration up to 16 cm. The ViewFlex Plus has similar profile with tissue penetration up to 21 cm. These two systems have Doppler capabilities and excellent maneuverability (anterior-posterior and left-right) for optimal imaging [9,10].

The ICE is distinctive to the computed tomography scan (CT) and MRI because of the real-time imaging during the procedure. Therefore, ICE provides real-time feedback for the device manipulation and the relationships with target structure [8]. Although transthoracic echocardiography (TTE) is also a real-time imaging, it is limited by various factors as obesity, emphysema, patient's position, respiratory cooperation and shadowing by echogenic materials. And inherently, visualization of structure far from the apex is not satisfactory. The anatomic information of interatrial septum (IAS) is insufficient, as it is only shown as a linear structure. In contrast, the ICE can be placed in the nearest point or in neighboring chamber where it exhibits the full advantages of near field imaging.

Lessons from other noncoronary procedures using ICE

For the procedural guiding, the transesophageal echocardiography (TEE) is generally accepted as the best

imaging modality. Still, there is no evidence that ICE is better than TEE in imaging aspect. However, the unique advantages of ICE in variable situations made it another efficient guiding modality. In reports about percutaneous ASD closure, freedom from the general anesthesia was emphasized as the major advantage of ICE compared with TEE [11,12]. Not only it avoided complications of general anesthesia, but Boccalandro *et al.* [12] reported that ASD closures using ICE presented shorter procedural time (47 ± 8 vs 35 ± 6 min, $p < 0.001$) and catheterization laboratory time (92 ± 18 vs 50 ± 12 min, $p < 0.001$) compared with those using TEE. And a TEE specialist was not needed thus to save a professional fee [11,12]. Moreover, occasionally TEE machine can block the fluoroscopic motion, and the probe hide fluoroscopic images; whereas the ICE is free from all these interruptions to the procedural flow. In reports about transcatheter aortic valve replacement, the ICE helped precise positioning of balloon and prosthetic valve, thus to reduce procedural time, radiation exposure and use of radiocontrast agents [13]; therefore, patients using ICE presented significantly lower incidence of acute kidney injury [14]. For the paravalvular leakage, currently the best imaging modality is TEE. Because the targets are usually tiny and occasionally concealed in acoustic shadow of prosthetic valve, it is technically demanding to affirm the wire passage and adequate closure. Although Ruiz *et al.* [15] reported the successful deployment of occluder in 42 of 49 (86%) lesions, Sorajja *et al.* [16] presented the moderate to severe remnant leakage in 30 of 126 (25%) patients. In this challenging area, ICE has some potentials; it would be suitable to visualize the orifice at the anterior side of prosthetic aortic valve (opposite side of TEE probe) [17], could be placed in nearest point to the orifice to ensure complete closure. All these are yet to be firm; however, the featured advantages of ICE to complement the TEE is noticeable in emerging procedures. The percutaneous mitral commissurotomy (PMC) including trans-septal puncture (TSP) is usually performed only under fluoroscopic guidance. The ICE also showed advantages in TSP, the standard views from RA provided powerful near field images of IAS [18]. The ICE presented the detailed anatomic feature of IAS (aneurysm, lipomatous hypertrophy, double layered septum and presence of patent foramen ovale [PFO]) and specified the puncture point [9]. Accordingly, it helped to avoid the potential risk of injury in adjacent structures (1–4% [19]). Therefore, the TSP seems to be the best indication of ICE; currently, the TSP under ICE is expanded to ablation for atrial fibrillation and MitraClip® implantation [7]. Ultimately, it would be applicable to biopsy of the left heart tumor.

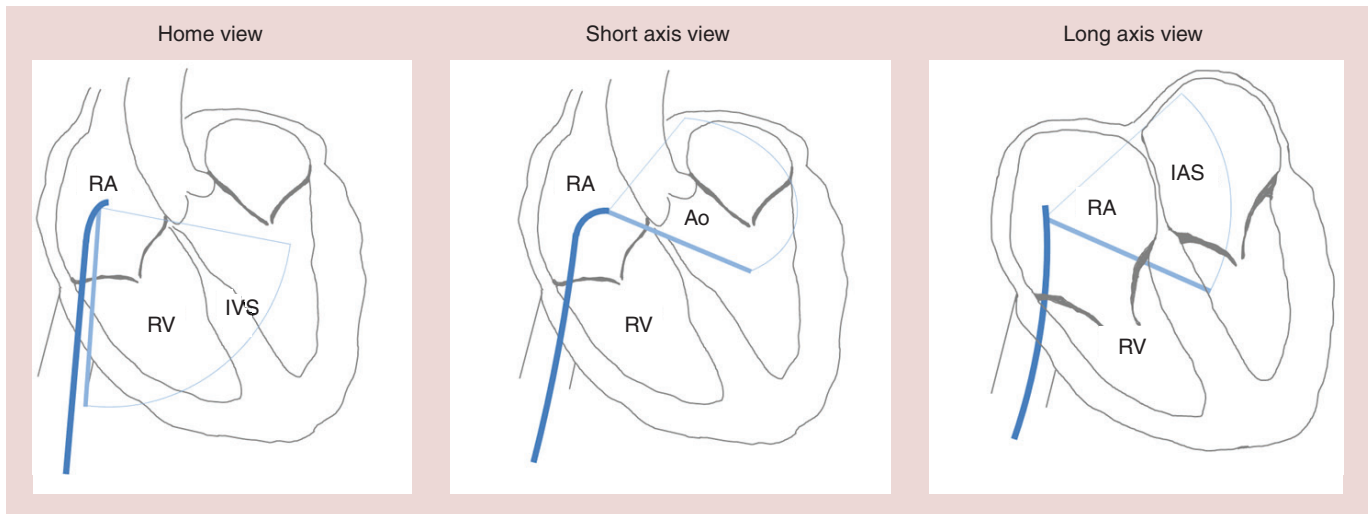


Figure 1. The standard views from the right atrium. Each panel from the left demonstrates the home view, long axis and short axis view, respectively. As the catheter has good maneuverability; the operator can adjust the position and angle, and fluently make the optimal images.

Ao: Aorta; IAS: Interatrial septum; IVS: Interventricular septum; RA: right atrium; RV: Right ventricle.

Advantages of ICE specific to cardiac biopsy

As the imaging capability of ICE is best for the near field, it is the key to place the catheter tip at the nearest point to the target. Once ICE is placed in optimal position, it presents specific advantages for cardiac biopsy. First, it points for the site of tissue sampling considering extent and thickness of tumor and surrounding anatomies [8]. Marrouche *et al.* [20] reported in their patients underwent pulmonary vein isolation under fluoroscopy that the catheter locations were apart from true ostium by 5 ± 3 mm. For an example, lymphoma presents rapid proliferation and degeneration; occasionally, the biopsy is nondiagnostic according to location and depth of tissue sampling. Also enough tissue volume is good to special staining. Therefore, the ICE would be advantageous to enhance the diagnostic power of cardiac biopsy. Second, the ICE is the real-time imaging for the direction, curve and angle of devices; helps to deliver the operator's manipulation. Remind that 'biting or slippage' determines 'success or failure' of whole biopsy procedure. Third, for an example of angiosarcoma with predilection to RA and infiltrating nature [2,21]; the operator should be extremely cautious to mural laceration and cardiac tamponade. In the previous report of our group [22], the ICE helped operator to avoid perforation of RA wall, and at the same time it ensured the adequate depth of tissue sampling (Figure 2). Bedside TTE is generally used for emergent evaluation, however, it needs at least several minutes for a personnel and machine to be available. Also it contaminates the sterile procedural field. Using ICE, the operator may adjust the depth of sampling, monitor the complication in real-time and make prompt decision for pericardiocentesis if needed.

Safety, technology & feasibility issues

Although the benefits are thought to outweigh, there are also potential risks in ICE inherent to catheter based modality. The overall complication rate was reported to be 4% in all cases [23]. Femoral or jugular venipuncture can cause vascular injury or bleeding. Manipulation of catheter can irritate endocardium and provoke arrhythmias. And the introduction of catheter can cause endothelial damage and thrombosis leads to venous and pulmonary thromboembolism, and even systemic embolism in presence of PFO. In technical aspect, far field imaging is another limitation. The left atrial far wall, appendage and left ventricular lateral walls are challenging sites for ICE. However, new phased-array systems provide imaging depth of 16–21 cm and good maneuverability to adjust the imaging fields [8–10], and the recently introduced intracoronary sinus ICE will be helpful for left heart imaging. Although the real-time 3D imaging in TTE and TEE presented benefits in terms of procedural success, complication and procedural times [7], it is still developing in ICE. The economic burden is another issue. Alborias *et al.* [11] reported in their 40 patients underwent ASD device closure that the ICE group presented higher hospital charges compared with the TEE group (USD 24,595 \pm 4616 vs 19,473 \pm 2613, $p < 0.001$). They also pointed out that the ICE group saved professional fee (for general anesthesia and TEE), therefore the global charges including hospital and professional charges were balanced. However, surely the cost of catheter system (USD 2000–2500) is an important barrier to the general use of ICE [8,11]; there should be individual consideration for various national circumstances regarding professional fee, health insurance system, and strategy for re-use of device. In educa-

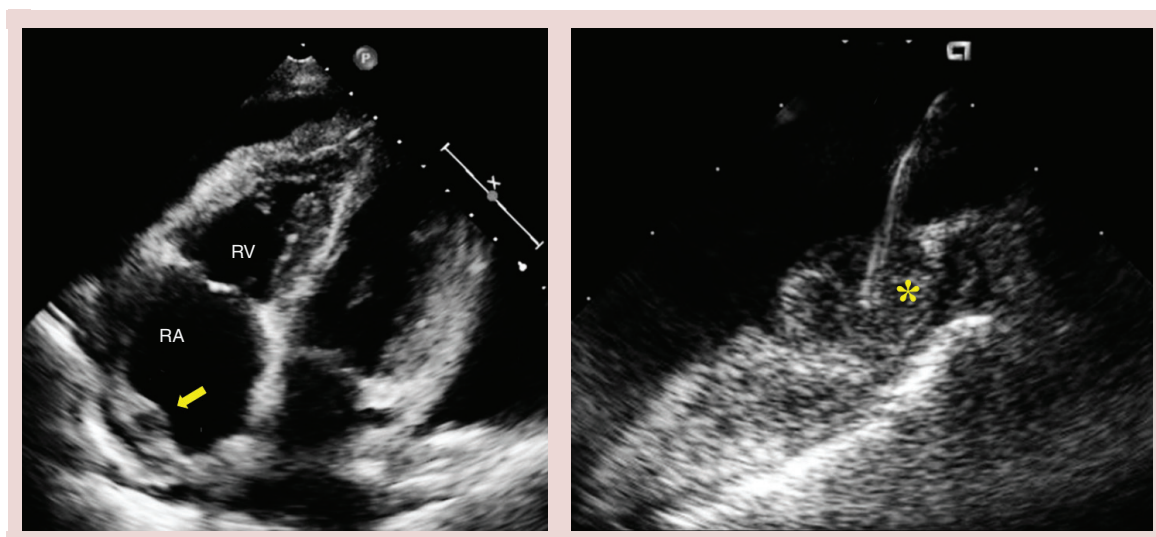


Figure 2. Intracardiac echocardiography-guided biopsy of the right atrium tumor. The transthoracic echocardiography showed infiltrating tumor in RA posterior wall (arrow, left panel). The ICE ensured the optimal sampling from the core (asterisk, right panel) without penetration of the thin target. Finally, the pathology specimen proved angiosarcoma.

ICE: Intracardiac echocardiography; RA: Right atrium; RV: Right ventricle.
Modified with permission from [22].

tional aspect, general standard has not been established as those in TTE or TEE. Instead, the vendors provide some educational courses including hands-on training.

Conclusion

ICE is an emerging imaging modality that has potential to fulfill various needs for guiding cardiac biopsy.

It provides clear intracardiac imaging for target and devices, therefore helps adequate tissue sampling which enhances the diagnostic power. Continuous monitoring for complication and freedom from general anesthesia are important advantages. Also it helps to reduce procedural time and radiation exposure. Although there are technical and economic issues to be

Executive summary

Background

- Cardiac biopsy is essential in both primary and secondary (metastatic) cardiac tumors.
- Primary cardiac tumors show variable prognosis according to the pathology, also the metastatic cardiac tumor is treated according to the pathologic diagnosis.
- Fluoroscopy is an insufficient imaging modality for cardiac biopsy, therefore intracardiac echocardiography (ICE) is expected to be key to enhance this procedure.

Overview of device & advantages

- The commonly available systems are the AcuNav® and ViewFlex Plus® with 64-element phased-array beam, 5.0–10.0 MHz, and penetration up to 16–21 cm.
- ICE surpasses transthoracic echocardiography, which is limited by obesity, emphysema, respiration and acoustic shadowing by echogenic materials.
- ICE helps to avoid general anesthesia, to reduce procedural time and radiation exposure, and to save professional fees.
- ICE provides clear near field images of the tumor and surrounding structures for precise targeting.
- ICE provides real-time feedback for device manipulation for adequate tissue sampling.
- ICE provides continuous monitoring for complications during procedure.

Safety & economic issues

- The overall complication of ICE was reported as 4% including vascular injury, bleeding, arrhythmias and thrombosis.
- The cost of the catheter system (US\$ 2000–2500) is an important economic barrier.

Conclusion

- ICE-guided biopsy for cardiac tumor has potential benefits outweighing the risk and cost, therefore its role will expand as the clinical evidence accumulates in a near future.

solved, and large-sized clinical evidence is still lacking; the prospect of ICE in cardiac biopsy is encouraging in a near future as the evidence accumulates.

Future perspective

- With the rapid technical advances in devices, the far field imaging and real-time 3D imaging of ICE will be improved.
- Accompanied with trans-septal puncture and intracoronary sinus ICE, the experiences for the left heart biopsy will be increased.
- The interventional cardiologist and trainees will have the chance for more generalized and standardized education.

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