

How to? / Nasıl yapalım?

(Interventional Cardiology / Girişimsel Kardiyoloji)

How to perform an endomyocardial biopsy?*Endomiyokardiyal biyopsi nasıl yapılmalı?***Carsten Tschöpe, M.D.,^{#†‡} Behrouz Kherad, M.D.,[#] Heinz-Peter Schultheiss, M.D.***[#]Department of Cardiology, Charité, Campus Virchow, Berlin, Germany^{*}Institut für Kardiale Diagnostik und Therapie (IKDT), Berlin, Germany[†]Berlin Center for Regenerative Therapies (BCRT), Berlin, Germany[‡]German Centre for Cardiovascular Research (DZHK), Center, Berlin, Germany**Introduction**

Endomyocardial biopsy (EMB) plays an integral part in the diagnosis of myocarditis and inflammatory cardiomyopathies. The underlying causes of myocarditis occur at a cellular level, and no other diagnostic technique can establish the nature of the etiological agent. Moreover, apart from detection of inflammation or viral genomes, EMB adds important prognostic information during the follow-up that can influence therapeutic decisions. The 2013 ESC position statement on myocardial disease advocates the application of EMB in the evaluation of patients with suspected myocarditis and inflammatory cardiomyopathies, as well as for patients with rapidly advancing cardiomyopathy refractory to conventional therapy. However, despite this recommendation, there exist a restriction of EMB procedures in some centers mainly due to safety concerns. We could recently show, analyzing 3048 EMB taken from the right ventricle (RV), that the risk of major complications including cardiac tamponade and AV block requiring permanent pacemaker implantation was as low as 0,12%, whereas no deaths were registered. A multicenter study analyzing over 4000 EMBs mainly of the left ventricle (LV) over a 28-year period also showed very low complication rate of 0.33%. These data and similar studies

show, that both right and left ventricle EMBs, when performed by experienced operators, have very low complication rates.

Technique

Vascular access for RV EMB is usually through the right or left femoral or right internal jugular vein. LV EMB is preferred through the right or left femoral artery or the right radial artery. The diagnostic value of LV versus RV EMB has been analyzed in various studies. We showed recently that both procedures are similar when assessing inflammation or viral genome in the myocardium. We strongly believe, that for these analysis's not the localization, but the number of taken EMBs is important to get a definite diagnosis and to reduce the sampling error. In our center, we got the best results when one EMB for histology, promptly fixed in 10% formalin, and up to two EMBs for immunohistochemical analysis and six EMBs for molecular biological investigations, all stored in RNA later tubes at room temperature, were taken. The sample size should be at least 1–2 mm. However, since we could demonstrate that at least morphological changes such as interstitial fibrosis and cardiac collagen type I expression were more reliably found in LV EMB, we perform routinely LV EMB especially in cases where a coronary angiogram is performed prior to LV biopsy

Tschöpe, C., and Kherad, B., contributed equally to this article.

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Correspondence: Dr. Carsten Tschöpe, Augustenburger Platz 1, 13353 Berlin, Germany.

Tel: +49 (30) 450-553711 e-mail: carsten.Tschoepe@charite.de

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to rule out relevant coronary artery disease as the underlying pathology for heart failure.

EMB is performed in a supine position under local anesthesia. The patient must be monitored with 3-lead ECG, non-invasive blood pressure monitoring and oxygen saturation. International normalized ratio (INR) of <1.5 is required before the EMB, and anticoagulation therapy should be discontinued 16 hours before and 12 hours after the procedure. Echocardiogram is recommended before and immediately after the procedure to exclude pericardial effusion. If possible, we recommend a 12h–24h telemetric observation after the procedure. Furthermore, we recommend an in house transthoracic echocardiography prior to the biopsy to confirm the diagnosis of cardiomyopathy, estimation of the LV ejection fraction, LV hypertrophy, detection of altered myocardial texture and to rule out any obstacles for left ventricular EMB such as a diameter of the lateral LV wall <8 mm or non-compaction cardiomyopathy, LV thrombus or relevant aortic valve stenosis.

Transradial left ventricular EMB

Following local anaesthesia, a 6F sheath (Radifocus Introducer II, 10 cm, Terumo, Japan) is introduced into the right radial artery. Upon sheath introduction every patient receives 3000 IU unfractionated heparin and 5 mg verapamil i.a. to prevent radial artery occlusion or spasm. A 5 F pigtail catheter (Boston Scientific,

USA) is now advanced into the LV. A long J-wire (260 cm, 0.03500) is advanced over the pigtail catheter to hold the ventricular position, the pigtail and the 6F radial sheath are removed, and a 7.5F sheathless multipurpose guiding catheter (MP1.0, Asahi Intecc, Japan) is introduced, whereas the dilatator is removed as soon as the sheathless guiding catheter reaches the ascending aorta. Following removal of the dilatator the guiding catheter is carefully advanced over the wire into the LV cavity. The J-wire is now removed and a Y-connector (Copilot, Abbott Vascular, USA) is connected. The correct position of the guiding catheter tip is checked in 20° left anterior oblique (LAO) projection with the tip of the catheter pointing to the lateral LV wall. Once the positioning of the catheter is confirmed 6 ml of contrast agent are injected to visualize the distance of the tip to the lateral LV wall (Figure 1a). The guiding catheter should not touch the wall. Prior to the biopsy, activated clotting time is checked (ACT: 200–250 sec) to prevent thromboembolism during the procedure. After the biotom forceps (B-18110; 1100 mm, 1.8 mm, Medizintechnik Meiners, Germany; Figure 2) have been washed in water to prevent air embolism, they are inserted into the MP1.0 guiding catheter via the Y connector. This step is very important and has to be repeated each time the forceps are introduced.

Several biotoms from different companies are available, which differ in prize, the possibility of re-

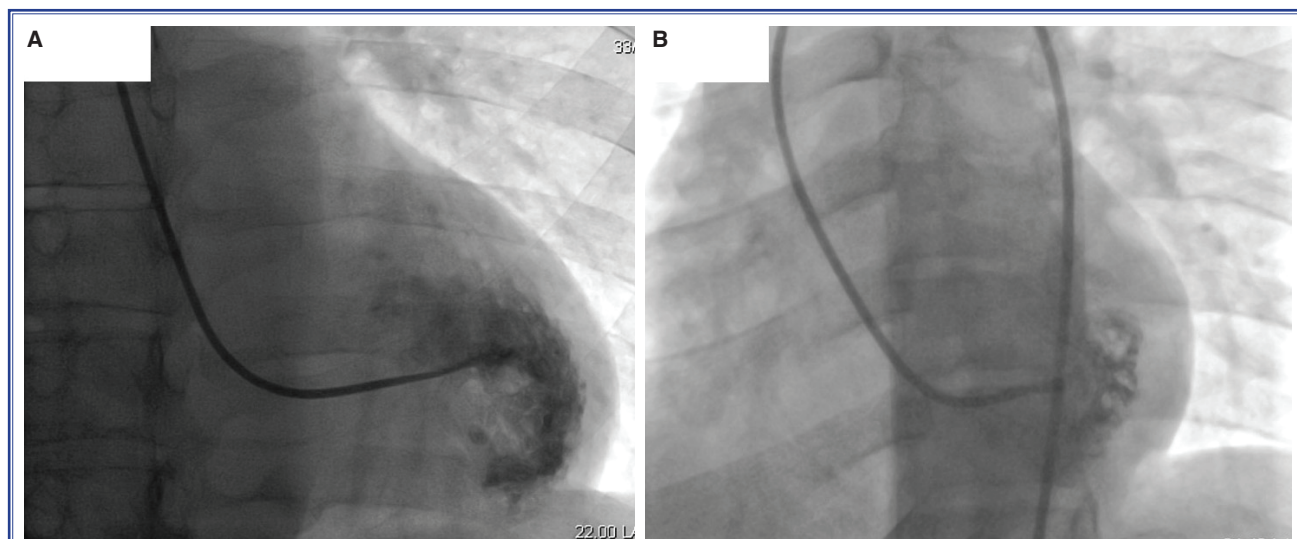


Figure 1. LV angiography fluoroscopy in LAO 20° view with injection of 6 ml contrast agent to visualize the position of the 7.5 F MP-1 guiding catheter inside the left ventricle (tip pointing to the lateral LV wall). **(A)** Transradial approach. **(B)** Transfemoral approach.

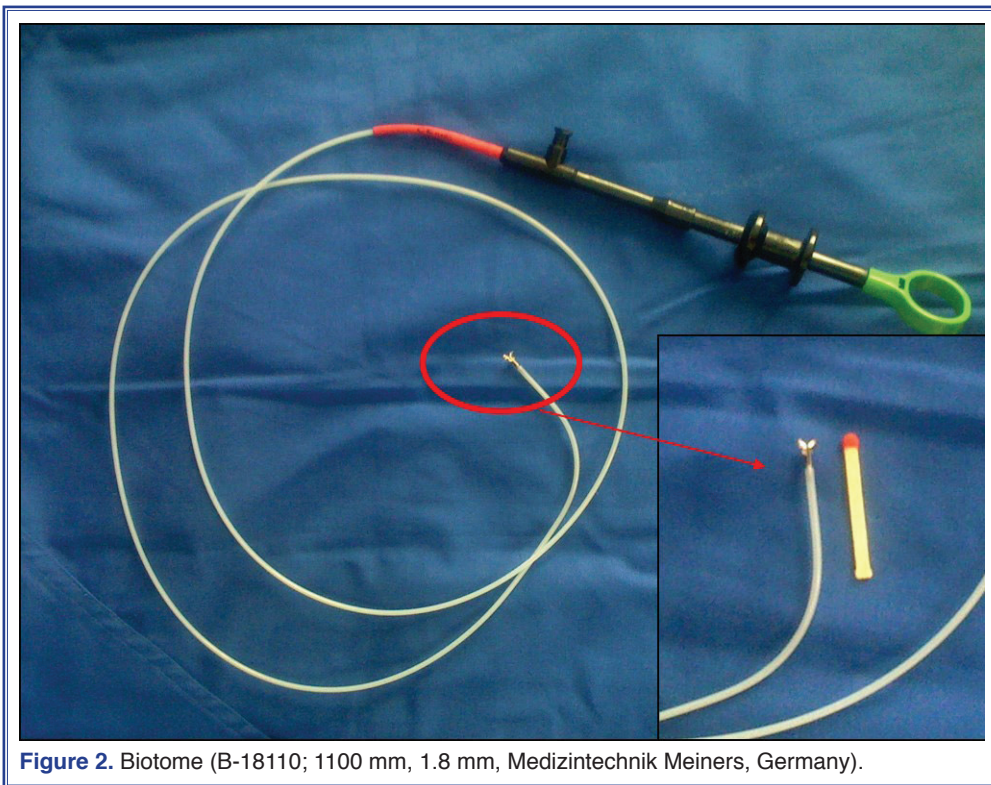


Figure 2. Biotome (B-18110; 1100 mm, 1.8 mm, Medizintechnik Meiners, Germany).

sterilization, and in stiffness and flexibility, respectively. We use a very flexible biotome (B-18110, Medizintechnik Meiners, Germany). It has a 6F diameter and a length of 1100 mm. The 2 closed jaws have a total diameter of 1.8 mm, a length of 2.8 mm, and a volume of 4.5 mm³. Compared with other biotomes, it has a more flexible polytetrafluoroethylene (Teflon) tube instead of an inflexible steel spiral and smaller jaws.

The forceps of the biotome are advanced under fluoroscopy close to the tip of the guiding catheter. The forceps are opened inside the guiding catheter and carefully advanced toward the lateral left ventricular wall. As soon as resistance is felt or fluoroscopically seen, the jaws are closed and the forceps immediately retracted into the guiding catheter (Video 1*). Upon completion of the procedure, the sheathless guiding catheter is removed and a vascular closure device (TR Band, Terumo, Japan) is applied for haemostasis. Each patient receives low dose aspirin for 4 weeks to prevent embolisms from the area of biopsies.

Transfemoral left ventricular EMB

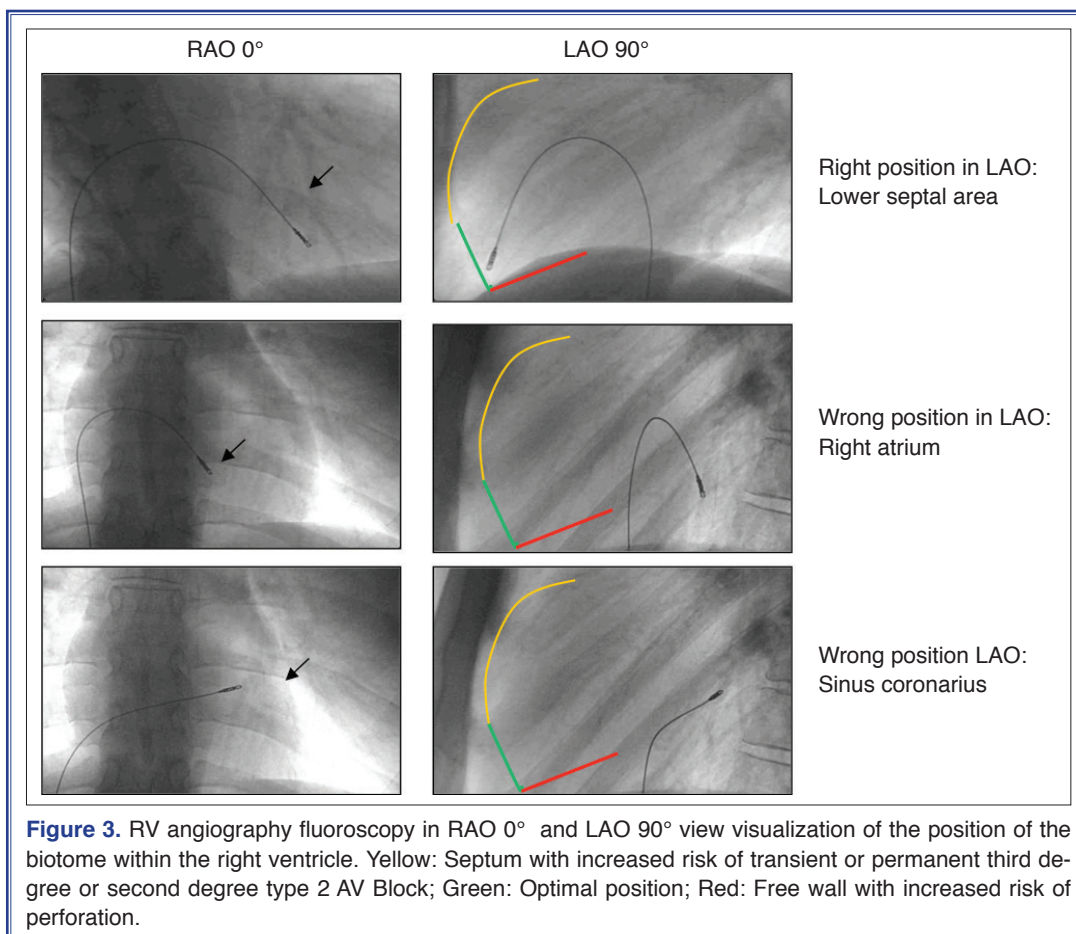
Following local anaesthesia, an 8 F sheath (Radifocus Introducer II, 10 cm, Terumo, Japan) is introduced

into the right or left femoral artery. Upon sheath introduction every patient receives 3000–4000 IU unfractionated heparin (ACT: 200–250 sec). A 5 F pigtail catheter (Boston Scientific, USA) is now advanced into the LV. A long J-wire (260 cm, 0.03500) is advanced over the pigtail catheter to hold the ventricular position, the pigtail is removed and an 8 F multipurpose guiding catheter with side holes (MP1.0 SH, Medtronic, USA) introduced, and the guiding catheter is carefully advanced over the wire into the LV cavity. The J-wire is now removed and a regular Y-connector (Copilot, Abbott Vascular, USA) is again connected. The following steps are identical to the transradial approach (Figure 1b).

Upon completion of the procedure, the guiding catheter and the 8 F sheath are removed and an 8 F vascular closure device is applied for haemostasis. Each patient receives a low dose aspirin prophylaxis for 4 weeks, too.

Transfemoral right ventricular EMB

For this access no heparinisation or in aspirin prophylaxis is recommended. Following local anaesthesia, an 8 F sheath (Arrow Flex, 30 cm, Tereflex, USA) is introduced into the right or left femoral vein. The



left vein access might have an advantage in younger patients where the position of the heart is often steep. We use the described biotome of Meiners (B-18110), which allows due to its flexibility an easy modulation of the Teflon tube according to individual anatomy of the patient. In contrast to others, we do not use a guiding catheter under these conditions, which would destroy the flexibility of the tube and increase the perforation risk. Principally, we do not recommend a use of any stiff biotomes for RV biopsies. Under fluoroscopic control at 0° right anterior oblique (RAO) projection the biotome is advanced to the right atrium. After careful turning into the direction of the tricuspid valve it can be advanced into the RV. The ideal position of the biotome in the RV has to be checked at 90° LAO (Figure 3). It is not recommended to take RV biopsies at RAO views; since these views cannot exc-

lude that the biotome is still in the (large) right atrium or was introduced into the sinus coronaries (Figure 3). Before opening the forcep of the biotome one has to be sure, that the biotome is not touching the wall to prevent uncontrolled tissue damage. Usually a short backward move of the biotome is enough to open the forcep in the cavum of the RV, followed by a new forward move with now an opened forcep to the lower part of septal wall to get the biopsy. Taking biopsies at higher parts of the septum would increase the risk of AV-blocks, especially in patients with established left bundle block. Upon completion of the procedure, the biotome and the 8 F sheath are removed and haemostasis is established by manual compression for several minutes.

**Supplementary video file associated with this article can be found in the online version of the journal.*