Study Title:

Contrast-enhanced intracardiac echocardiography for localization of myocardial scar during ablation of ventricular tachycardia

NCT# 03212326

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Subsequent revised versions: none.

Objective

We sought to compare areas of scar marked on 3D-integrated ICE with abnormal electrogram sites in patients with cardiomyopathy (CM) and VT.

Design

Prospective, single-arm study enrolling 24 subjects.

Methods

We prospectively evaluated 24 pts (mean age 67 ± 14, 89% male) with CM (83% ischemic) undergoing VT ablation. ICE contours of the left ventricle were drawn on Carto at baseline and again during infusion of echo contrast (perflutren). Areas of akinesis, thinning, or abnormal echogenicity were labeled as scar, and compared with the voltage map (sites <1.5 mV defined LVR).

INCLUSION

Age > 18 years

Undergoing catheter ablation of likely reentrant VT

Planned use of intracardiac echocardiography (ICE)

EXCLUSION

Contraindication to perflutren (Definity) echo contrast: known right-to-left, bidirectional, or transient right-to-left cardiac shunts; known hypersensitivity to perflutren

STUDY PROTOCOL

Informed consent is to be obtained prior to procedure.

After initial standard catheters are placed for electrophysiologic study (including ICE catheter), ICE imaging is optimized and echo contrast will then be infused:

Contrast protocol (Fay Lin, M.D.)

Echocardiographic contrast agents have demonstrated safety and efficacy for enhancement of chamber opacification in transthoracic echocardiography (Mulvagh 2008). Intravenous

echocardiographic contrast has also been utilized for evaluation of left atrial appendage thrombus prior to electrophysiologic procedures (von der Recke G 2002, Ruiz-Arango 2008, Donal E 2008).

Definity contrast (0.5 ml of Definity agitated and diluted in a 50-mL bag of normal saline) will be administered as a continuous intravenous infusion (12 ml/h) through a large bore peripheral intravenous line (20 Fr). The infusion rate will then be adjusted to obtain homogeneous LV cavity opacification without attenuation of distal segments. Pulse emission frequency (MHz) and mechanical index (MI) will be adjusted to obtain optimal endocardial and myocardial definition. Gain control and time-gain compensation will be adjusted at the noise floor during contrast imaging. 3D ICE images will be acquired after image optimization. No more than 0.5 ml total of Definity will be administered to any patient during one study.

ICE imaging and localization of myocardial scar (Chris Liu, M.D.)

With optimized contrast-enhanced ICE, myocardial scar will be localized and marked using the 3-dimensional mapping system (CartoSound) which is used standardly during these procedures.

Post-procedure analysis

Scar areas identified and localized using contrast-enhanced ICD will be compared qualitatively (location via the 17-segment model of the left ventricle as well as categorization of endocardial, intramyocardial, and epicardial) and quantitatively (measured areas on the 3D maps) with the scar areas identified and localized using the conventional 3D electroanatomic map (obtained in the same patient per standard of care). Wilcoxon test will be used to compare paired data for each patient.

Hypothesis

There is high correlation between scar areas identified by contrast-enhanced ICE and scar areas identified by conventional electroanatomic mapping.

Contrast safety

A large body of relevant published clinical data establishes the safety of approved and experimental ultrasound contrast agents (Herzog CA 2008). Adverse effects have been reported for all approved contrast agents; they are usually infrequent and mild and may include headache, weakness, fatigue, palpitations, nausea, dizziness, dry mouth, altered sense of smell or taste, dyspnea, urticaria, pruritus, back pain, chest pain, or rash, or a combination of these effects. However, allergic and potentially life threatening hypersensitivity reactions may occur rarely. Therefore, patients should be monitored for hypersensitivity reacitons under the direction of a physician experienced in the management of hypersensitivity reactions. Echocardiographic contrast consists of micronized bubbles and is unrelated to iodinated

contrast; as such, renal insufficiency or renal failure is not a contraindication to use of echocardiographic contrast.

In 2008, the FDA reviewed the safety of echocardiographic contrast and implemented the following contraindications for Definity and other contrast agents:

- Contraindicated in right-to-left, bidirectional, or transient right-to-left cardiac shunts
- Contraindicated in hypersensitivity to perflutren
- Patients with pulmonary hypertension or unstable cardiopulmonary conditions must have additional monitoring of vital signs, electrocardiography, and cutaneous oxygen saturation for 30 minutes after administration.

In this study, contrast imaging with intracardiac echocardiography will be performed prior to atrial septal puncture. Patients with right to left or bidirectional shunts observed on intracardiac echocardiography or who report hypersensitivity will not undergo contrast imaging. All patients will be observed for complications in the electrophysiology laboratory after contrast administration.

Scientific BACKGROUND

Ventricular tachycardia (VT) is a life-threatening arrhythmia which occurs frequently in the setting of structural heart disease, most often as result of myocardial fibrosis or scar. Catheter ablation is often performed to treat recurrent VT, but is predicated on precise localization of myocardial scar, as scar is often the source of VT. Currently during VT ablation procedures the identification of scar is based on electroanatomic mapping where bipolar voltage criteria have been established (i.e., bipolar electrogram voltage < 1.5 mV is considered scar). However this definition is purely based on electrical signal information and so has significant limitations: 1) there has not been definitive establishment of the sensitivity and specificity of this threshold for defining scar in comparison with tissue; 2) a detailed 3-D map created by time-consuming movement of the mapping catheter must be obtained in order to assess the existence and location of the scar; 3) only scar on the surface in contact with the mapping catheter (most often endocardial) may be definitively identified, whereas there may be intramyocardial or epicardial scar that would not be identified unless the mapping catheter makes direct contact with those areas which may involve additional risky access (epicardial) or even impossible (intramyocardial). For these reasons it would be very helpful to have another method to identify and localize myocardial scar during a VT ablation procedure. Cardiac MRI has been validated for identifying and localizing scar, but would not be recommended for many patients

due to presence of ICD (implantable cardioverter-defibrillator) devices in these patients. Contrast-enhanced echocardiography has been validated to identify myocardial scar (Montant 2010), and intracardiac echocardiography (ICE) is standardly used in VT ablation procedures. In this study, we will assess the utility of contrast-enhanced ICE to identify and localize myocardial scar real-time during VT ablation procedures. The advantage of having scar areas precisely identified with ICE would be more expeditious localization of scar without involving the fluoroscopy exposure of electroanatomic mapping.

Citations

Ruiz-Arango A, Landolfo C. A novel approach to the diagnosis of left atrial appendage thrombus using contrast echocardiography and power Doppler Imaging. Eur J Echocardiogr. 2008 9:329-33

Donal E, Sallach JA, Murray RD, Drinko JK, Jasper JE, Thomas JD, Klein AL. Contrast-enhanced tissue Doppler imaging of the left atrial appendage is a quantitative measure of spontaneous echocardiographic contrast in atrial fibrillation. Eur J Echocardiogr. 2008 9:5-11

Von der Recke G, Schmit H, Illien S, Luderitz B, Omran H. Use of transesophageal contrast echocardiography for excluding left atrial appendage thrombi in patients with atrial fibrillation before cardioversion.

Herzog CA. Incidence of adverse events associated with use of perflutren contrast agents for echocardiography. JAMA 2008; 299:2023

Montant P, Chenot F, Goffinet C, et al. Detection and quantification of myocardial scars by contrast-enhanced 3D echocardiography. Circ Cardiovasc Imaging. 2010;3:415-423.

STATISTICAL ANALYSIS PLAN

The scar locations suggested by ICE were compared to those obtained with traditional electroanatomic mapping after completion of the study by an electrophysiologist with training in both electrophysiology, intracardiac ultrasound imaging, and transthoracic echocardiography. Scar areas identified and localized using contrast-enhanced echo will be compared qualitatively (location via the 17-segment model of the left ventricle as well as categorization of endocardial, intramyocardial, and epicardial) with the scar areas identified and localized using the conventional 3D electroanatomic map (obtained in the same patient per standard of care).

This is a descriptive study. We will present percent of subjects with scar as detected by intracardiac echo without contrast, with intracardiac echo enhanced with contrast, with voltage mapping, and percentage of ventricular tachycardia mapped to the scar segments on echo and voltage maps. We will compare these percentages using the Kruskal-Wallis test in order to assess 3 groups with likely non-parametric data. Data analysis will be performed using MedCalc version 13.2.