

## Contrast Echocardiography for the Evaluation of Tumors and Thrombi

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Contrast echocardiography is based on intravenous injection of microbubbles that act as blood flow tracers and increase ultra-sound signal. Contrast agents have shown to improve cardiac cavities opacification and endocardial border delineation in addition to helping perfusion evaluation. Contrast echocardiography has recently been used to evaluate cardiac masses. In this report we will describe three cases evaluated by contrast echocardiography: a left atrial myxoma (benign tumor), a lung adenocarcinoma metastasis (malignant tumor), and one thrombus. Contrast echocardiography showed to be valuable in the diagnosis of the different types of cardiac masses.

### Introduction

Contrast echocardiography is a technique that utilizes contrasting agents based on injected microbubbles via a peripheral intravenous injection to improve echocardiographic signals<sup>1,2</sup>. The use of contrast echocardiography has additionally show value in detecting alteration in ventricular global function as well as in determining changes in segmental mobility and of myocardial perfusion both at rest and stress<sup>3-5</sup>. Currently, the validity of this method for differential diagnosis of cardiac masses is argued based on their vascular pattern analysis<sup>6,7</sup>. With the general understanding that benign tumors have lower vascularization, that thrombi are avascular, and that malignant tumors are highly irrigated<sup>7</sup>, three cases will be described that illustrate how contrast echocardiography can be used to evaluate these masses.

### Case Report

#### Case 1

A 55-year old, asymptomatic male patient presented upon routine examination cardiac auscultation changes in the presence of systolic and diastolic murmurs in the mitral focal point. The patient was submitted for a transthoracic

### Key Words

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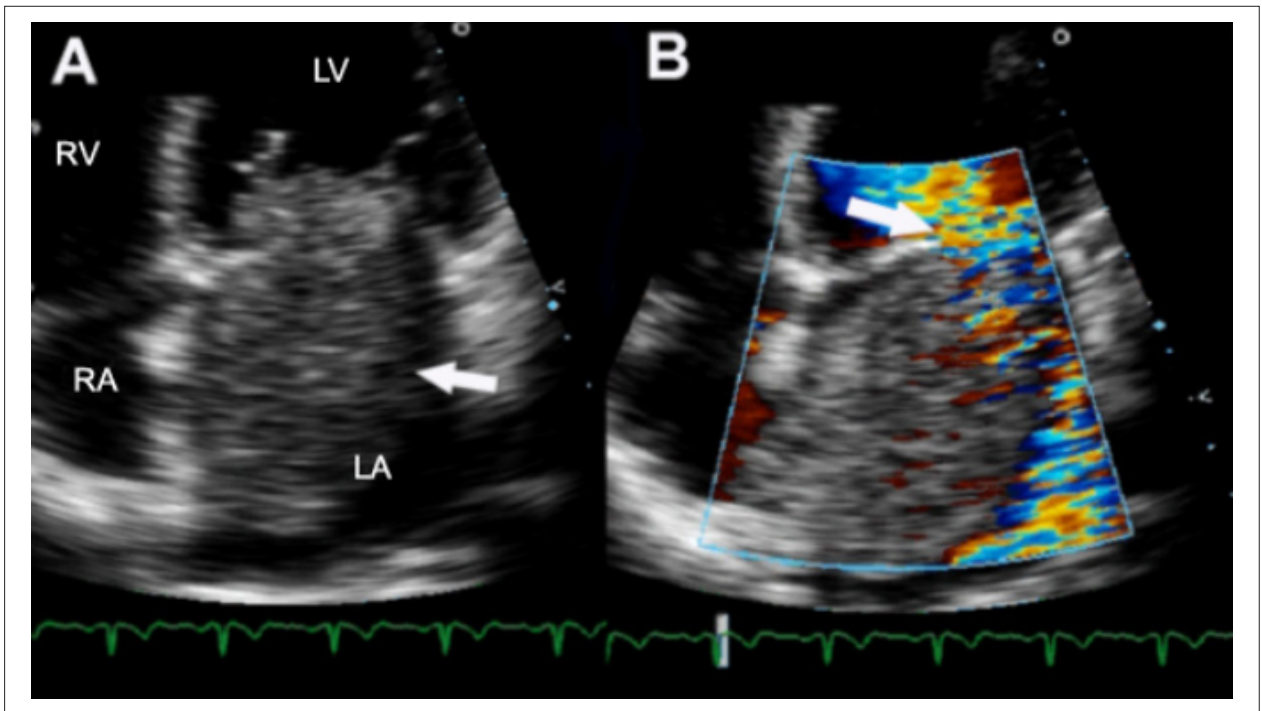
echocardiogram which subsequently showed a large mass within the left atrium. Surgical removal of the mass was recommended, the patient refused surgical intervention. Two years later, the patient returned with symptoms of cardiac insufficiency. Physical exam revealed normal systemic arterial blood pressure, 4+/6+ systolic murmur and 2+/6+ diastolic murmur in the mitral region were noted. Electrocardiogram (ECG) showed left atrium overload. Transthoracic echocardiogram showed a large rounded mobile mass with irregular contours, adhering to the inter-atria septum suggestive of left atrial myxoma. The mass was projected toward the mitral valve during ventricular diastole, thus generating flow obstruction (functional stenosis) and poor coaptation of mitral valve cusps resulting in mitral insufficiency (Figure 1). Contrast echocardiography was performed using an albumin based microbubbles (PESDA - Perfluorocarbon Exposed Sonicated Dextrose and Albumin) and the SONOS 5500 (Philips Medical Systems, Bothell, WA) echocardiograph, with real perfusion imaging in real time (Power Modulation). The use of contrast echocardiograph permitted delineation of the mass borders. For the purpose of vascularization evaluation, a high energy ultra-sound pulse (flash) was used to destroy contrast, followed by the analysis of time-dependent mass re-filling by the microbubbles. As is illustrated in Figure 2, slow contrast filling of the mass was observed suggestive of low vascularization of the tumor mass, typical of benign tumors. The patient was submitted for surgery, confirming a diagnosed left atrial myxoma.

#### Case 2

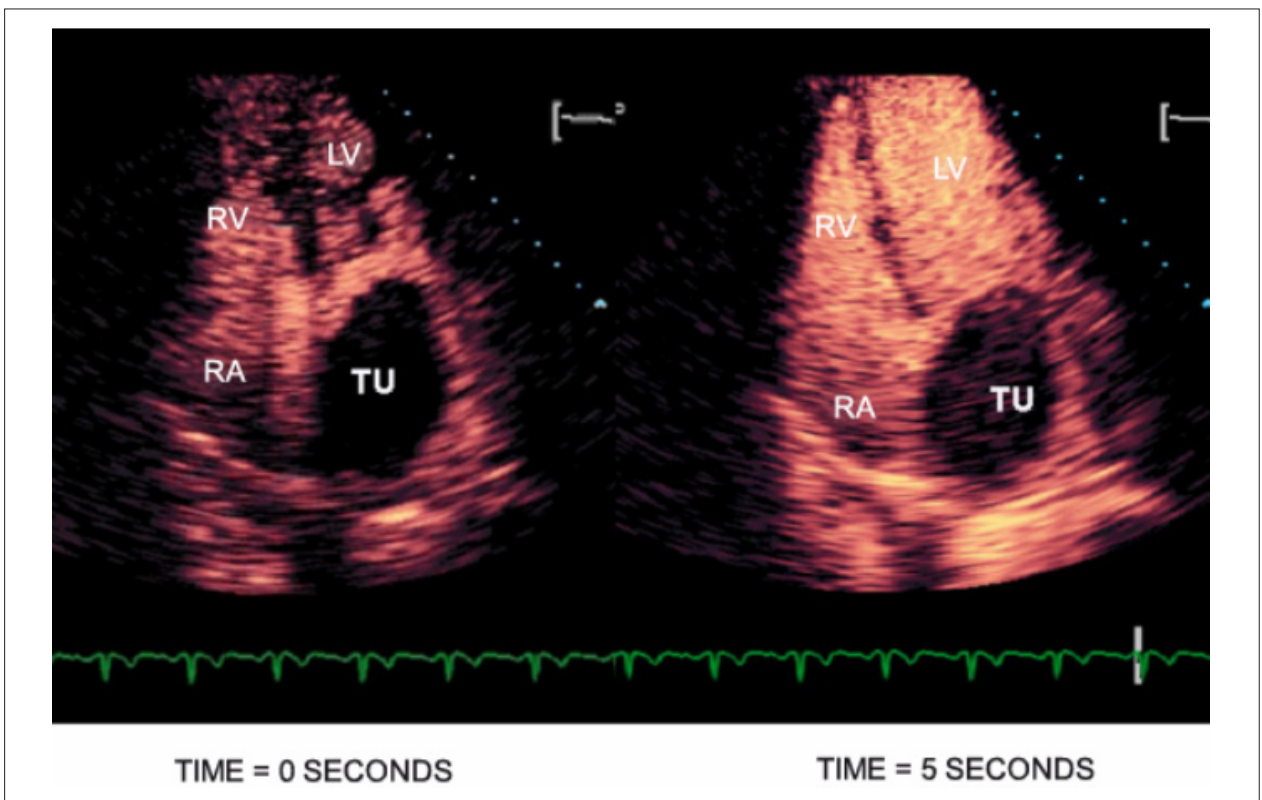
A 42-year old female patient presented for medical services, having a history of pre-cordial pain and dyspnea upon low exertion. Physical exam revealed normal systemic arterial pressure, 2+/6+ systolic murmur in the pulmonary foci, and an unaltered pulmonary auscultation. No significant changes were observed on standard 12-lead electrocardiogram. Transthoracic echocardiogram showed a localized mass between the aortic arch and pulmonary artery (Figure 3), with irregular borders. An echocardiography with PESDA contrasting agent permitted identification of the rapidly filled with mass with contrast, suggesting an intense vascularization (Figure 4). The patient was submitted for other complementary exams, with resultant diagnosis of pulmonary adenocarcinoma. The mass identified by echocardiography corresponded to a metastatic malignant tumor.

#### Case 3

A 64-year old, male patient, with a history of systemic arterial hypertension, Type 2 Diabetes Mellitus, a smoking

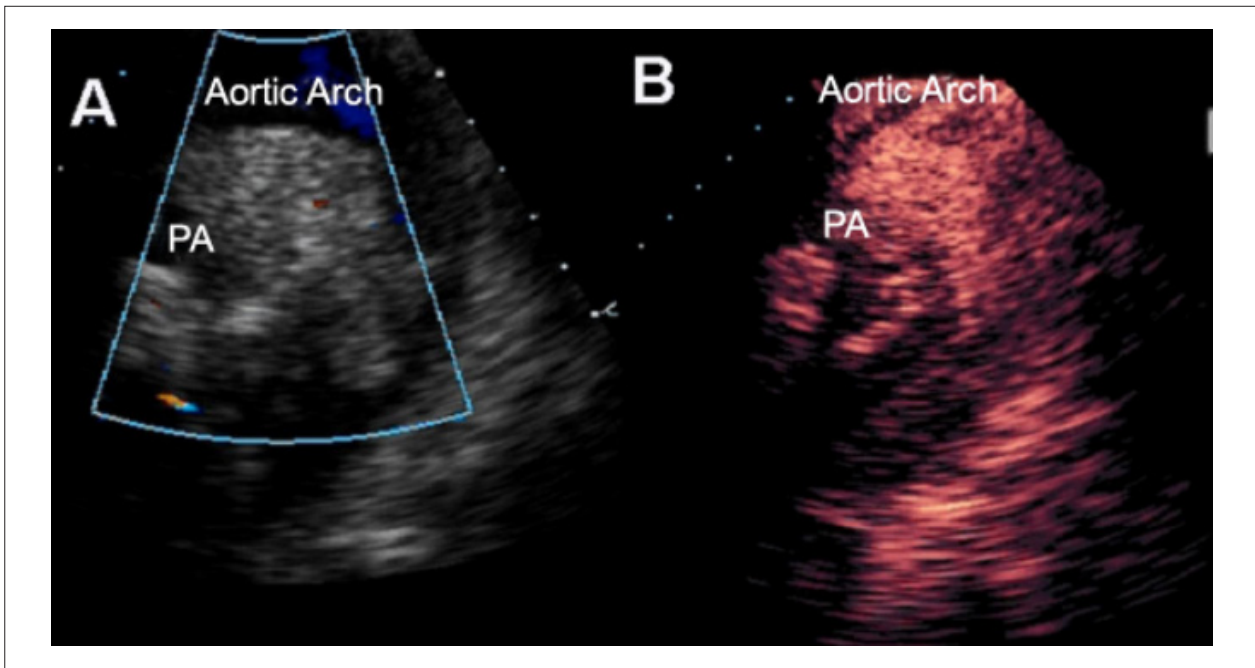


**Figure 1** - ECG showing large roundish mass in left atrium, adhered to interatrial septum, projecting towards the mitral valve during ventricular diastole and resulting in obstruction to ventricular filling (Panel A, arrow); Color flow mapping (Panel B) shows turbulent flow during systole (mitral failure); LV - left ventricle, RV - right ventricle, RA - right atrium, LA - left atrium.

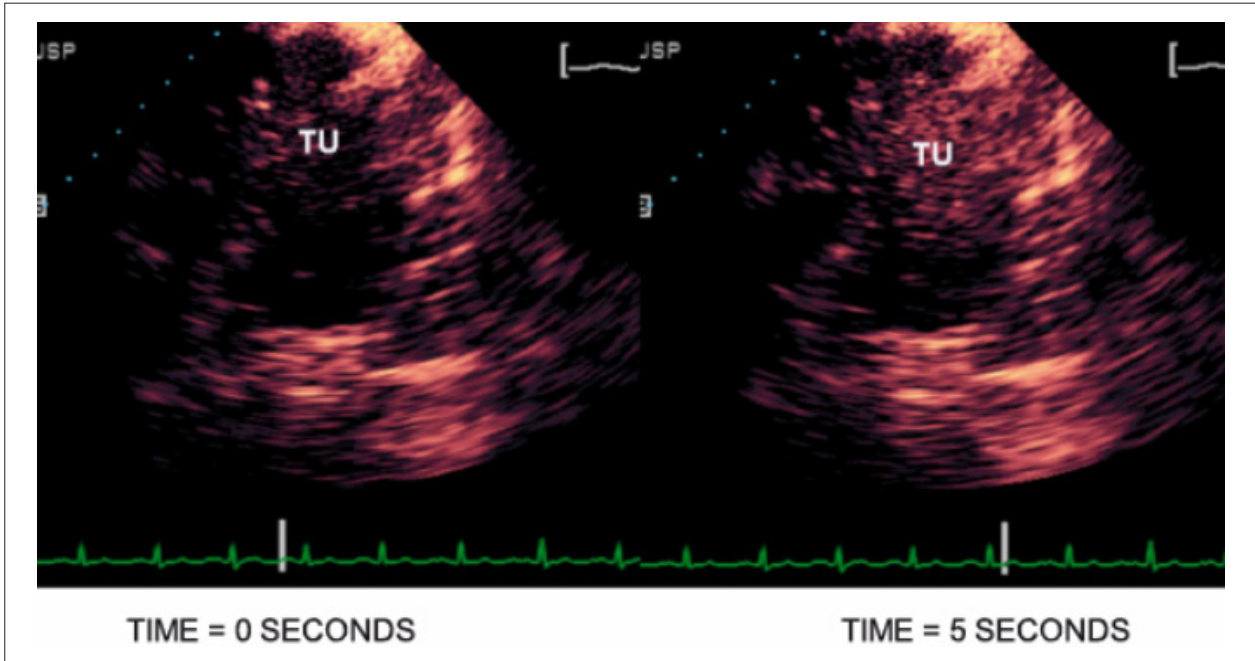


**Figure 2** - Contrast echocardiography showing delineation of ventricular mass borders; For the purpose of vascularization evaluation high energy ultra-sound was used (flash) to destroy contrast, followed by refilling analysis; No contrast was observed immediately after flash inside the mass (left panel); After 5 seconds the mass shows mild contrast filling (right panel), indicating low vascularization; LV - left ventricle, RV - right ventricle, RA - right atrium, TU - Tumor

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**Figure 3** - Transsthoracic ECG showing irregular contour mass between aortic arch and pulmonary artery (A); Echocardiographic contrast injection demonstrated mass was filled with contrast, which suggests a tumor (B); PA - pulmonary artery.



**Figure 4** - Contrast echocardiography showing that immediately after high energy ultra-sound pulse contrast signals could be seen inside the tumor (left panel); After 5 seconds, there is significant contrast filling (right panel) to indicate the tumor was highly vascularized.



habit, and myocardial infarction presented for medical services with complaints of dyspnea. Physical examination revealed blood pressure at 90 x 60 mmHg, pulmonary stertoration, 5+/6+ systolic murmur of the mitral valve, hepatomegaly with palpable liver at 4 cm from left costal border, and +/4+ edema in the legs. Twelve lead ECG demonstrated overload of the left chambers and an electrically inactive area in antero-septal wall. ECG showed significant ventricular dysfunction with anterior, septal, and apical akinesia, and imaging suggestive of an apical thrombus. Contrast echocardiography with PESDA permitted better delineation of the adhered apical ventricular mass while demonstrating likewise no filling of the same with contrast, confirming an apical thrombus (Figure 5). An oral anticoagulation was introduced and cardiac insufficiency medications were optimized.

Blood flow quantification inside the mass was performed for all three cases utilizing specific quantification software (Q Lab 4.0, Philips Medical Systems, Bothell, WA). Perfusion analysis is based on the capacity to measure mass refilling velocity by the microbubbles and the maximum intensity of contrast<sup>8</sup>. Therefore, the software provides the variable B; representing the mass filling time by contrast related to the degree of vascularization<sup>6</sup>. The greater the mass vascularization, the higher the corresponding B value.

Case 1 refers to a myxoma – a benign tumor, with higher prevalence in adult populations<sup>9</sup>, and accounting for 20-50% of all cardiac tumors. Contrast perfusion (case 1) analysis revealed a B of 0.86s<sup>-1</sup>. Case 2 is a secondary malignant

tumor (metastasis of a pulmonary adenocarcinoma), with a B of 10.47s<sup>-1</sup>. Case 3 is a thrombus with a B value of 0.45s<sup>-1</sup> (Figure 6). Therefore, a comparable observation exist between the type of cardiac mass its vascularization, and the corresponding B value.

## Discussion

Current contrast echocardiography indications include left ventricular opacity and delineation of endocardial borders in patients with suboptimal echocardiographic window<sup>1</sup>. With the recent development of more persistent micro-bubbles and associated advancements of ultra-sound techniques has contributed to both myocardial and cardiac mass perfusion studies. The concentration of microbubbles in the micro-circulation reflect the blood volume in the different regions of the heart and forms the basis for perfusion evaluation through contrast echocardiography.

Cardiac tumors are very rare with an incidence below 0.1% according to autopsies performed<sup>10</sup>. Tumors are classified according to their origin, histology type and growth site. Primary tumors originate start in the heart itself, while secondary tumors originate in other organs. As far as histological patterns, they may be benign or malignant. Finally, as for growth site, they may be classified as intracavitary, intramural, and intrapericardial<sup>11</sup>. Transthoracic echocardiographic exceed 90% sensitivity in diagnosing cardiac tumors<sup>9,12</sup> and provides information regarding size, shape, motility, fixation, relation with adjacent structures, and hemodynamic repercussions. However, differential

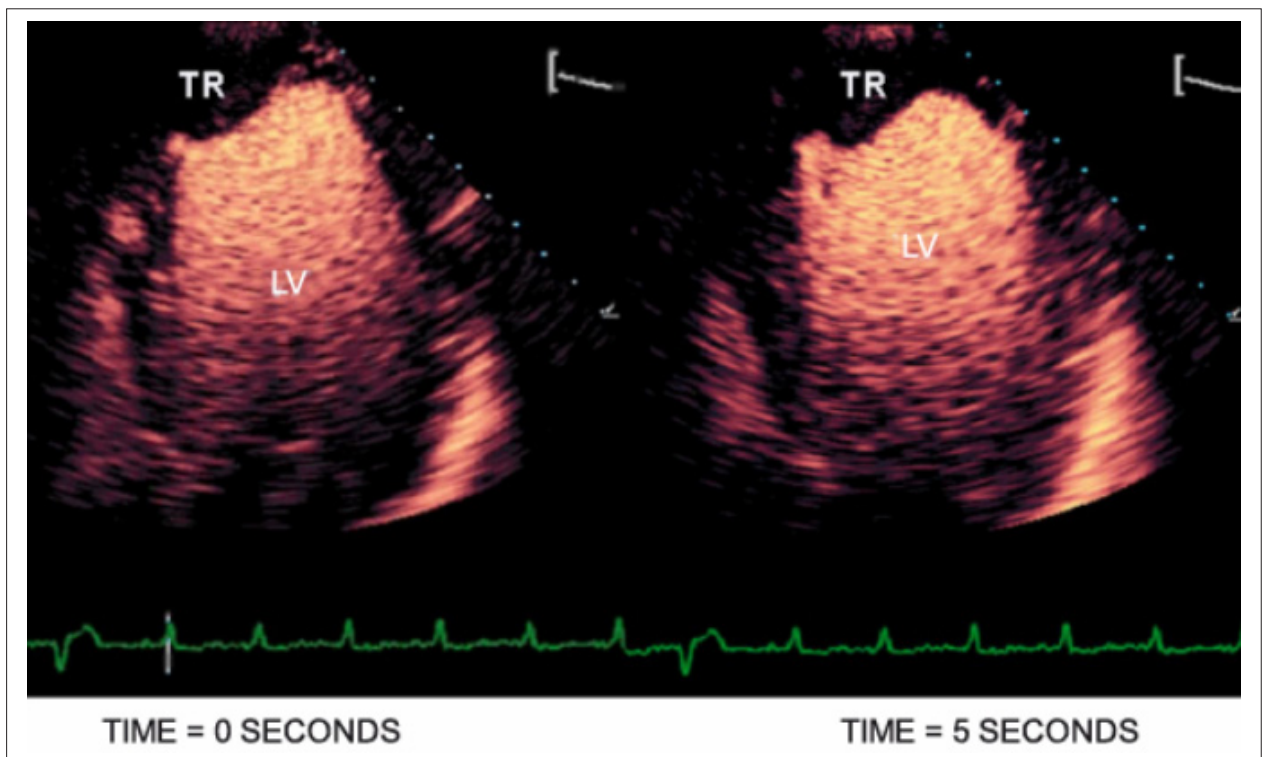
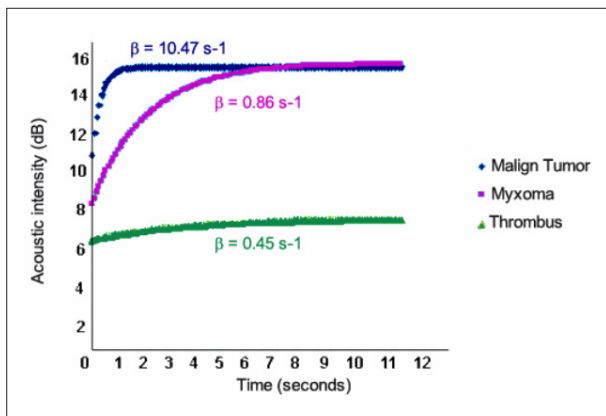


Figure 5 - Contrast echocardiography showing dilated left ventricle, with no contrast filling at ventricular apex (non-vascularized), suggesting apical thrombus.

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**Figure 6** - Curves: Maximum acoustic intensity and mass contrast filling velocity ( $\beta$ ) for each of the cases presented; Malignant tumor velocity showed to be much higher than benign tumor (myxoma); Thrombus quantification curve was flattened, thus indicating no time-dependent filling of microbubbles (vascularized mass).

diagnosis between cardiac benign and malignant tumors, and thrombi may be difficult to assess in some cases. Malignant tumors exhibit enriched vascularization allowing rapid cell tumor growth<sup>13</sup>. Benign tumors (on the other hand) have less vascularization when compared to malignant tumors with the exception of hemangiomas. Thrombi are generally avascular.

In this report we have demonstrated the differences between filling time using contrast echocardiography in cases of a benign tumor, a malignant tumor, and a cardiac thrombus. The report also illustrates the use of contrast echocardiography in evaluating the degree of cardiac mass vascularity. In conclusion, this technique may be a valuable tool for the analysis and differential diagnosis between malignant cardiac tumors, benign tumors, and thrombi. It should be emphasized, however, further studies are recommended regarding this topic.

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