

## Original Article

# Estimation of $T_2^*$ Relaxation Times for the Glandular Tissue and Fat of Breast at 3T MRI System

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**Purpose :**  $T_2^*$  relaxation time which includes susceptibility information represents unique feature of tissue. The objective of this study was to investigate  $T_2^*$  relaxation times of the normal glandular tissue and fat of breast using a 3T MRI system.

**Materials and Methods:** Seven-echo MR Images were acquired from 52 female subjects (age  $49 \pm 12$  years; range, 25 to 75) using a three-dimensional (3D) gradient-echo sequence. Echo times were between 2.28 ms to 25.72 ms in 3.91 ms steps. Voxel-based  $T_2^*$  relaxation times and  $R_2^*$  relaxation rate maps were calculated by using the linear curve fitting for each subject. The 3D regions-of-interest (ROI) of the normal glandular tissue and fat were drawn on the longest echo-time image to obtain  $T_2^*$  and  $R_2^*$  values. Mean values of those parameters were calculated over all subjects.

**Results:** The 3D ROI sizes were  $4818 \pm 4679$  voxels and  $1455 \pm 785$  voxels for the normal glandular tissue and fat, respectively. The mean  $T_2^*$  values were  $22.40 \pm 5.61$  ms and  $36.36 \pm 8.77$  ms for normal glandular tissue and fat, respectively. The mean  $R_2^*$  values were  $0.0524 \pm 0.0134$ /ms and  $0.0297 \pm 0.0069$ /ms for the normal glandular tissue and fat, respectively.

**Conclusion:**  $T_2^*$  and  $R_2^*$  values were measured from human breast tissues.  $T_2^*$  of the normal glandular tissue was shorter than that of fat. Measurement of  $T_2^*$  relaxation time could be important to understand susceptibility effects in the breast cancer and the normal tissue.

**Index words :** Breast · 3T MRI ·  $T_2^*$  relaxation times

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## INTRODUCTION

Quantitative measurement of relaxation parameters in MRI refers to MR relaxometry which implies the measurement of biophysical parameters through decoupling the different contrast mechanisms contributing to the overall MR signal. MR relaxation mapping is important to evaluate the tissue structure and function. Among the quantitative MRI parameters reflecting the local tissue environment, the relaxation times  $T_1$ ,  $T_2$ , and  $T_2^*$  are the fundamental components (1, 2). The longitudinal (or spin-lattice) relaxation time  $T_1$  is the decay constant for the recovery of the z component of

the nuclear spin magnetization,  $M_z$ , towards its thermal equilibrium value. The transverse (or spin-spin) relaxation time  $T_2$  is the decay constant for the component of  $M$  perpendicular to  $B_0$ . The  $T_2$  value is usually measured using a T2-weighted spin-echo or fast spin-echo sequence. So far, a few studies have measured  $T_1$  and  $T_2$  relaxation times for breast tissue at field strengths of 3T MR (4, 5).

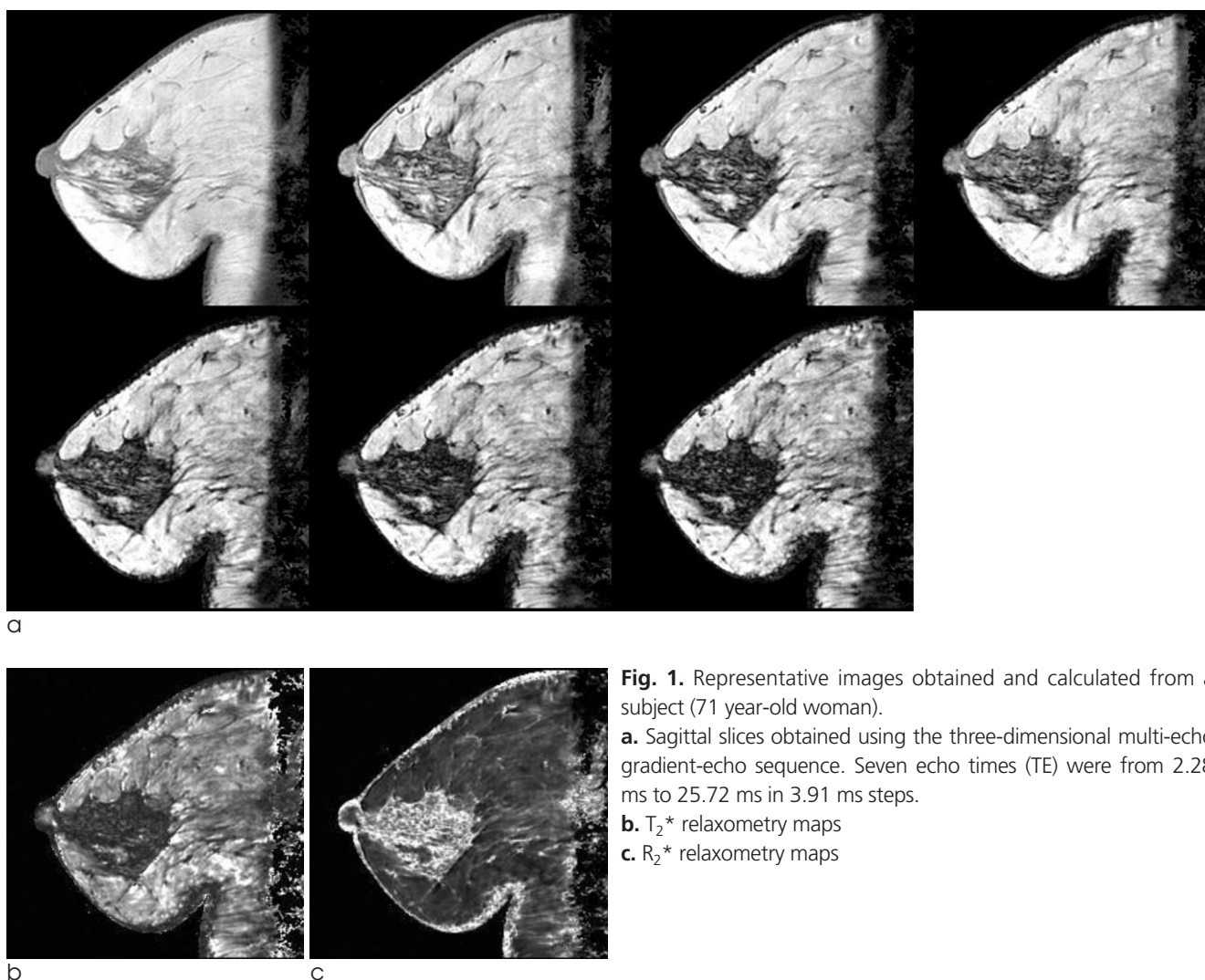
$T_2^*$  relaxation refers to decay of transverse magnetization caused by a combination of spin-spin relaxation and magnetic field inhomogeneity, which is usually much smaller than  $T_2$ .  $T_2^*$  relaxation is one of the main determinants of image contrast with gradient-echo(GRE) sequences and forms the basis for many MR applications, such as susceptibility-weighted (SW) imaging, perfusion MR imaging, and functional MR imaging (3). Magnetic field inhomogeneities from

susceptibility differences among tissues and materials cause faster  $T_2^*$  relaxation. Measurements of the  $T_2^*$  value were reported to evaluate oxygen amount (6), microbleeds (7), and functional changes (8) in human brains. However, currently there has been no report describing normal breast  $T_2^*$  relaxation time. The purpose of this study, therefore, was to provide  $T_2^*$  relaxation time of normal glandular tissue and fat of breast.

## MATERIALS AND METHODS

### Subjects

Fifty-two female patients (age  $49 \pm 12$  years; range, 25 to 75 years) between January 2012 and July 2013 were included in this retrospective study, which was



**Fig. 1.** Representative images obtained and calculated from a subject (71 year-old woman).

**a.** Sagittal slices obtained using the three-dimensional multi-echo gradient-echo sequence. Seven echo times (TE) were from 2.28 ms to 25.72 ms in 3.91 ms steps.

**b.**  $T_2^*$  relaxometry maps

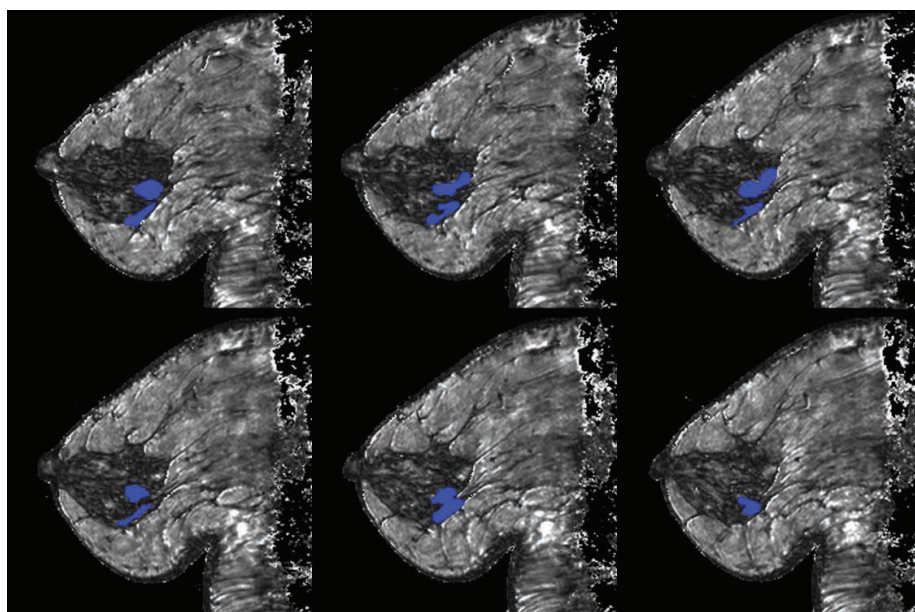
**c.**  $R_2^*$  relaxometry maps

approved by the local institutional review board. Premenopausal women were 28 and 24 patients were in their menopause status. Among these patients, 47 patients who had breast cancer underwent breast MRI as a preoperative staging work-up and remaining 5 patients performed breast MRI for various causes; one patient for screening examination as a uterine cervix cancer patient, two patients who had benign breast lesion such as nodular fasciitis and stromal fibrosis,

one patient for injection granulomas and one patient proceeded as follow up study for previous lumpectomy of breast cancer.

### MRI Acquisition

Scans were performed on a 3T MRI system (Achieva, Philips Healthcare, Best, The Netherlands) with four-channel breast coil for reception with patients in the prone position. The regular breast MR

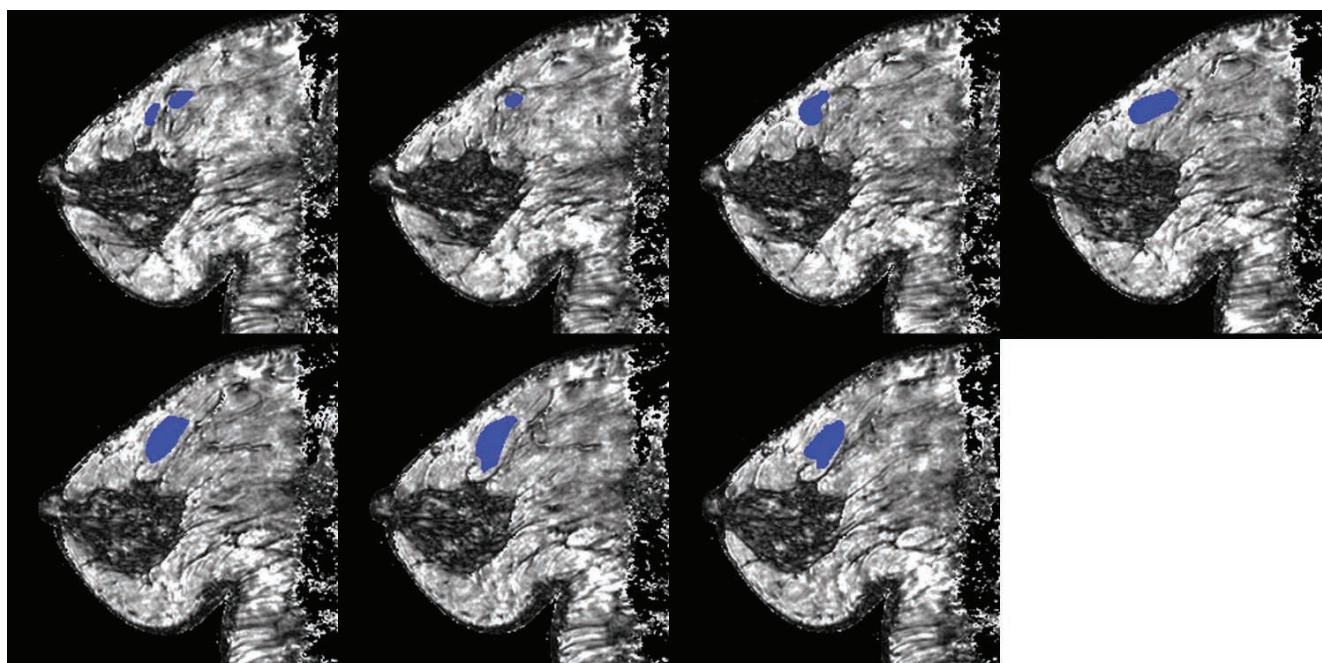


a

**Fig. 2.** Representative regions-of-interest overlaid in  $T_2^*$  map in the same subject of Fig. 1.

a. Fibroglandular tissue

b. Fat



b

imaging protocol in our institute included axial T1-weighted image (T1WI) and axial short inversion recovery (STIR) T2-weighted image (T2WI) in both breasts, axial three-dimensional (3D) dynamic contrast enhanced T1WI (DCE-T1WI) in both breasts, and 6-min delayed, postcontrast enhanced sagittal fat-suppressed T1WI (CE-T1WI) for both breasts. DCE-T1WI was obtained 20 times with 18.8 seconds each interval.

To measure  $T_2^*$  relaxation time, a 3D multi-echo gradient-echo sequence was acquired with sagittal slices (Fig. 1a). Seven echo times (TE) were from 2.28 ms to 25.72 ms in 3.91 ms steps. The imaging parameters were: repetition time (TR)=37.4 ms, flip angle=20°, field of view (FOV)=133 × 130 mm<sup>2</sup>, pixel size=0.55 × 0.55 mm<sup>2</sup>, matrix size=240 × 240, slice thickness=1.4 mm, the interesting gap= 1.4 mm, number of slices=105, the number of signals averaged (NSA)=1, and SENSE factor= 1.3.

### MRI Data Processing

To create voxel-based  $T_2^*$  and  $R_2^*$  maps, the post-processing was performed using a MATLAB software (Natick, MA, USA). Seven volumes of the sagittal images were aligned with respect to the first volume to correct any movement. The signals were fitted using below equation:

$$S(TE) = S_0 \exp(-TE/T_2^*)$$

where  $S_0$  is the equilibrium signal from the voxel and  $T_2^*$  is the relaxation time. The logarithm was taken for every voxel and the mono-exponential decay characteristics of the signal became a linear decline as echo increased. The MATLAB built-in function *polyfit* was used to perform a linear curve fit of the logarithmic signal and the  $T_2^*$  value for each voxel was generated. After the  $T_2^*$  map for each slice was produced, its inverse was calculated to create  $R_2^*$  maps (Fig. 1b, c).

To obtain  $T_2^*$  and  $R_2^*$  values of the normal glandular tissue and fat, the 3D regions-of-interest (ROI) were then drawn on the longest echo-time image (Fig. 2a, b). Volumetric ROIs were drawn by the one radiologist with 4 years (S.J.R.) experience in breast MR imaging. The  $T_2^*$  and  $R_2^*$  values for fat tissue was calculated from an average of five ROIs drawn in the

**Table 1.  $T_2^*$  and  $R_2^*$  Values in Glandular Tissue and Fat of Breast**

	Glandular Tissue	Fat
ROI size (voxel)	4818 ± 4679	1455 ± 785
$T_2^*$ (ms)	22.40 ± 5.61	36.36 ± 8.77
$R_2^*$ (1/ms)	0.0524 ± 0.0134	0.0297 ± 0.0069

Note.— Data present mean ± standard deviation over all subjects.

subcutaneous fat region. The size of the ROIs varied because they were drawn to maximize a region of the homogeneous tissue type. The same method was used to draw ROIs of the glandular tissue. Mean and standard deviations of the two parameters in ROIs for each subject were obtained for all subjects. Finally, those parameters were averaged over all subjects for the normal glandular tissue and fat of breast.

## RESULTS

The 3D ROI sizes were 4818 ± 4679 voxels and 1455 ± 785 voxels for the normal glandular tissue and fat, respectively. The mean  $T_2^*$  values were 22.40 ± 5.61 ms and 36.36 ± 8.77 ms for the normal glandular tissue and fat, respectively. The mean  $R_2^*$  values were 0.0524 ± 0.0134/ms and 0.0297 ± 0.0069/ms for the normal glandular tissue and fat, respectively (Table 1). Two sample T-test revealed statistically significant, long  $T_2^*$  value of fat compared with that of glandular tissue ( $p < 0.00001$ ) and also statistically significant difference of  $R_2^*$  value between those two tissue components ( $p < 0.00001$ ).

## DISCUSSION

Accurate information of relaxation times is the basis for the progress and optimization of MR imaging sequences. Currently, there are two reports (4, 5) explaining normative relaxation time data for 3T breast MRI, where only  $T_1$  and  $T_2$  were discussed, however, none was reported about  $T_2^*$  relaxation time. In this study, we performed  $T_2^*$  relaxometry maps and our result revealed longer  $T_2^*$  value for fat in the breast compared with that of fibroglandular

tissue. A previous study (4) also demonstrated that the T<sub>2</sub> value for adipose tissue was almost three-fold longer than that of fibroglandular tissue resulting in much greater T<sub>2</sub> contrast between adipose and fibroglandular tissue.

We could also speculate our relative long T<sub>2</sub>\* value result of fat from the histological difference. Adipose tissue of breast is loose connective tissue composed mostly of adipocytes and some stromal vascular fraction. In contrast, fibroglandular tissue of breast is composed of various components such as terminal duct lobular unit, ductules, intralobular connective tissue, interlobular connective tissue and major ducts. Even though lobules and intralobular connective tissue are formed with loose myxomatous stroma with secretion in various levels of ducts, interlobular stroma which is composed of dense, more collagenous connective tissue forms network in breast resulting more compact and various tissue components which may induce magnetic field inhomogeneities.

T<sub>2</sub>\* relaxation is a combined effect of true T<sub>2</sub> relaxation and relaxation caused by magnetic field inhomogeneities. Following equation expresses their relation where  $\gamma$  is the gyromagnetic ratio:  $1/T_2^* = 1/T_2 + \gamma \Delta B_{\text{inhom}}$ , or  $1/T_2^* = 1/T_2 + 1/T_2'$ , where  $1/T_2' = \gamma \Delta B_{\text{inhom}}$ , and  $\Delta B_{\text{inhom}}$  is the magnetic field inhomogeneity across a voxel (9). Magnetic field inhomogeneity can be classified as macroscopic (intervoxel) and microscopic (changing within a voxel) (10). Macroscopic inhomogeneity can be caused by deoxyhemoglobin in tiny veins, by air-tissue interfaces, or by metallic implants. On the other hand, paramagnetic contrast agents, blood products, or iron deposits are the causes of microscopic inhomogeneity (11).

Knowledge of T<sub>2</sub>\* relaxation mapping would be a help in breast tumor and tissue characterizations such as microhemorrhage and microcalcification. Furthermore, in functional aspect of breast cancer, as T<sub>2</sub>\* reflects the macroscopic inhomogeneity caused by deoxyhemoglobin, oxygen consumption could be another important future point of view in understanding and planning of breast cancer diagnosis and treatment. As the 1/T<sub>2</sub> is referred to as the transverse relaxation rate (R<sub>2</sub>), 1/T<sub>2</sub>\* can be expressed as R<sub>2</sub>\*. The difference between R<sub>2</sub>\* and R<sub>2</sub> may suggest oxygen effects in tissue. This could presume the response and result of radiation therapy, affecting the

prognosis. Methods to alter tumor-tissue oxygenation and/or to measure the induced changes would be strong aids in the oncologic management of cancers. Radiation sensitivity is markedly lowered in hypoxic cells since oxygen is involved in the fixation of radiation-induced DNA damage, and loco-regional tumor control is adversely affected in patients with hypoxic tumors. Hypoxia also leads to reduced sensitivity towards chemotherapeutics since drug delivery is reduced in hypoperfused hypoxic areas and hypoxic cells are quiescent, making drugs that target dividing cells ineffective (12).

There were several limitations of this study. First, although we carefully drew ROIs to minimize contaminations of different tissues, ROI of the fibroglandular tissue may contain fat in the fatty breast. Therefore, T<sub>2</sub>\* and R<sub>2</sub>\* values of the fibroglandular tissue may not represent the pure value of the tissue. Second, we only used 7 echoes to measure the maps. However, it should be better to use more echoes to improve the fitting result. Finally, we only included normal tissues in this study. It should evaluate those maps in breast cancer. Currently, we are evaluating the T<sub>2</sub>\* values in several types of breast cancers.

In conclusion, we performed T<sub>2</sub>\* relaxometry map in breast tissue using the 3T MRI system. T<sub>2</sub>\* of the normal glandular tissue was shorter than that of fat. Measurement of T<sub>2</sub>\* relaxation time could be important to understand susceptibility effects in the breast cancer and the normal tissue.

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### 3테슬러 자기공명영상기기에서 유방의 유선조직과 지방조직의 T<sub>2</sub>\*이완시간 측정

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**목적:** T<sub>2</sub>\*이완시간은 조직의 고유한 특징을 반영하는 자화율 정보를 내재하고 있다. 본 연구는 3테슬러 자기공명영상 기기에서 유방의 정상 유선조직과 지방조직의 T<sub>2</sub>\*이완시간을 알아보고자 하였다.

**대상과 방법:** 52명의 여자환자에서 (나이, 49 ± 12세; 범위, 25세~75세) 삼차원 경사예코연쇄를 이용하여 각 일곱 개 에코 자기공명영상들을 얻었다. 에코시간은 3.91 ms단계에서 2.28 ms에서 25.72 ms사이 범위였다. 화적소를 기초로 T<sub>2</sub>\*이완시간과 R<sub>2</sub>\*이완율 지도는 각 개체에서 선형곡선맞춤을 이용하여 계산되었다. T<sub>2</sub>\*값과 R<sub>2</sub>\*값을 얻기 위하여 유방의 정상 유선조직과 지방조직에 삼차원 관심영역을 표시하였다. 모든 개체에서 이러한 변수들의 평균치를 계산하였다.

**결과:** 유방의 정상 유선조직과 지방조직에 삼차원 관심영역 크기는 각각 4818 ± 4679 화적소와 1455 ± 785 화적소 였다. 평균 T<sub>2</sub>\* 값은 유방의 정상 유선조직과 지방조직에서 각각, 22.40 ± 5.61 ms 와 36.36 ± 8.77 ms 였다. 평균 R<sub>2</sub>\*값은 유방의 정상 유선조직과 지방조직에서 각각, 0.0524 ± 0.0134/ms와 0.0297 ± 0.0069/ms 였다.

**결론:** 유방의 정상 유선조직과 지방조직에서 T<sub>2</sub>\*값과 R<sub>2</sub>\*값을 측정하였다. 유방의 정상 유선조직의 T<sub>2</sub>\*값은 지방조직의 T<sub>2</sub>\*값보다 짧게 나타났다. T<sub>2</sub>\*이완시간의 측정은 유방암과 정상 유방조직에서의 자화율 효과를 이해하는데 도움을 줄 것이다.

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