

## Original article

## Computing quantitative indicators of structural renal damage in pediatric DMSA scans

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## ABSTRACT

**Objectives:** The proposal and implementation of a computational framework for the quantification of structural renal damage from <sup>99m</sup>Tc-dimercaptosuccinic acid (DMSA) scans.

The aim of this work is to propose, implement, and validate a computational framework for the quantification of structural renal damage from DMSA scans and in an observer-independent manner.

**Materials and methods:** From a set of 16 pediatric DMSA-positive scans and 16 matched controls and using both expert-guided and automatic approaches, a set of image-derived quantitative indicators was computed based on the relative size, intensity and histogram distribution of the lesion. A correlation analysis was conducted in order to investigate the association of these indicators with other clinical data of interest in this scenario, including C-reactive protein (CRP), white cell count, vesicoureteral reflux, fever, relative perfusion, and the presence of renal sequelae in a 6-month follow-up DMSA scan.**Results:** A fully automatic lesion detection and segmentation system was able to successfully classify DMSA-positive from negative scans (AUC=0.92, sensitivity=81% and specificity=94%). The image-computed relative size of the lesion correlated with the presence of fever and CRP levels ( $p<0.05$ ), and a measurement derived from the distribution histogram of the lesion obtained significant performance results in the detection of permanent renal damage (AUC=0.86, sensitivity=100% and specificity=75%).**Conclusions:** The proposal and implementation of a computational framework for the quantification of structural renal damage from DMSA scans showed a promising potential to complement visual diagnosis and non-imaging indicators.

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## Cómputo de indicadores cuantitativos de daño renal estructural en imágenes DMSA pediátricas

## RESUMEN

**Objetivos:** En el presente trabajo se propone, implementa y valida un entorno computacional de cuantificación de imágenes con <sup>99m</sup>Tc-ácido dimercaptosuccínico (DMSA) con el objetivo de obtener indicadores cuantitativos del daño renal subyacente. Estos indicadores se validan en un contexto de imágenes DMSA pediátricas, dada su relevancia en el diagnóstico de pielonefritis aguda y cicatrices renales.**Materiales y métodos:** Partiendo de un conjunto de 16 imágenes DMSA positivas para daño renal y 16 controles apareados por edad y sexo, se proponen y calculan una serie de indicadores cuantitativos basados en el área relativa lesionada y la distribución de su histograma. Se implementan aproximaciones manuales y automáticas para dicho cómputo. Los indicadores obtenidos se correlacionan con otras variables clínicas de interés en este contexto, como la proteína C reactiva, la cuenta leucocitaria, el reflujo vesicouretral, la fiebre, la perfusión relativa, y la presencia de secuelas renales en la imagen DMSA a los 6 meses de seguimiento.**Resultados:** El sistema implementado de detección y cuantificación de lesiones renales obtuvo un rendimiento significativo discriminando las imágenes DMSA positivas de las negativas (AUC = 0,92, sensibilidad = 81% y especificidad = 94%). El indicador de área relativa de la lesión correlacionó con los niveles de proteína C reactiva y la presencia de fiebre ( $p<0,05$ ). Finalmente, un indicador derivado de las propiedades del histograma de la lesión obtuvo un rendimiento significativo en la detección de la presencia de secuelas renales (AUC = 0,86, sensibilidad = 100% y especificidad = 75%).

## Palabras clave:

DMSA

Daño renal

Análisis de imagen

Análisis cuantitativo

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**Conclusiones:** La propuesta e implementación de un entorno computacional para la obtención de indicadores cuantitativos a partir de imágenes DMSA muestra un potencial prometedor para complementar el diagnóstico visual.

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## Introduction

$^{99m}\text{Tc}$ -dimercaptosuccinic acid (DMSA) scans are a valuable nuclear medicine test in assessing renal morphology and structural damage. At the time of this writing, planar-image DMSA is the gold standard for the diagnosis of acute pyelonephritis and renal scars.<sup>1,2</sup> This particular clinical context is especially relevant within the pediatric population.<sup>3–5</sup>

An important limitation of this technique is that it does not distinguish accurately lesions that will spontaneously resolve from those which will cause permanent renal damage.<sup>6</sup> For that, a 6-month follow-up DMSA scan is needed in order to confirm a renal scar diagnosis, representing a major limitation both in clinical and economic terms.

DMSA scan evaluation by the trained physician remains purely visual. As in most medical imaging scenarios, while this approach is accurate enough in many cases, it suffers from inter- and intra-observer variabilities.<sup>7,8</sup> Additionally, its diagnostic product is descriptive and categorical, lacking a continuous modeling of the underlying renal damage.

With computational advances, the trend to try to complement the visual diagnostic products with image-derived quantitative and observer-independent parameters is spreading in the field. Although quantitative DMSA image analysis has been used in the field,<sup>9,25,26</sup> to the best of our knowledge, the computation of image-derived quantitative indicators of structural renal damage in DMSA scans has not been addressed by means of a comprehensive computational framework.

In this work, we propose for the first time a DMSA segmentation and quantification framework that seeks to provide clinically valuable indicators for the assessment of structural renal damage. In particular, we aim to compute image-derived quantitative and subject-independent parameters designed to model accurately the underlying renal pathophysiology observed in DMSA scans. The performance such indicators will be evaluated within three different contexts: automatic renal damage detection, indicators' correlation with non-imaging clinical data and early permanent renal lesion detection.

## Materials and methods

### Demographics and DMSA acquisition

A total of 16 pediatric DMSA scans with visually-diagnosed structural kidney damage, its 6-month follow-up DMSA scans, and 16 age- and sex-matched controls were obtained from the Philips

**Table 1**

Demographic and clinical data for the DMSA-positive group. Detailed information about the clinical relevance of these variables can be found in Ref. 10.

	Proportion of subjects with the parameter available	Mean $\pm$ standard deviation or proportion
Age (months)	16/16	27 $\pm$ 32
Sex (male/female)	16/16	12/16 females
Weight (kg)	16/16	10.8 $\pm$ 6.3
Fever (positive > 38 °C)	15/16	13/15 positive
C reactive protein (CRP) (mg/L)	15/16	112.5 $\pm$ 84.1
Leukocyte count (mil/mm <sup>3</sup> )	14/16	16.1 $\pm$ 7.6
Vesicoureteral reflux (positive/negative)	14/16	1/14 positive
Relative perfusion of the affected kidney (%)	16/16	47.6 $\pm$ 5.5
Chronic lesion, based on 6-month DMSA follow-up (positive/negative)	16/16	4/16 chronic lesion

Precedence workstation at the Nuclear Medicine department of Hospital de Sant Pau, Barcelona, Spain.

The 16 pathological DMSA scans showed clearly identifiable upper-pole single-kidney lesions, which are the most prevalent in our center. The image type of choice to be analyzed in this work is the white-background posterior projection of the DMSA acquisition.

Several demographic and clinical variables of interest in this context were also obtained for the 16 pathological cases (Table 1).

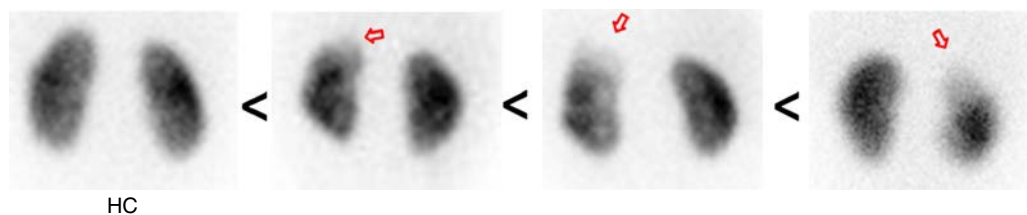
The 16 DMSA positive scans are intended to represent a wide spectrum of renal damage scenarios, making them a valuable set to test the efficiency of the proposed quantitative indicators at modeling the underlying renal pathology (Fig. 1).

### Computation of DMSA-derived quantitative indicators

In order to quantify the structural kidney damage (SKD) within the DMSA scans, two approaches (manual and automatic) were conducted regarding the image segmentation of the pathological areas. Then, from the obtained lesion's segmentation, a set of image-derived quantitative indicators is computed.

### Manual segmentation and quantification methodology

An expert-guided manual segmentation framework was custom-build using Matlab<sup>®</sup>.<sup>11</sup> Given the low resolution of the



**Fig. 1.** Four examples of DMSA scans illustrating the pathological spectrum to be modeled by the proposed quantitative indicators. HC: healthy control. The patient of the third scan suffered renal sequelae as opposed to the patients of the other two pathological scans. The illustrative conceptual ordering of the positive scans was based on visual inspection of the damaged area.

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