The Value of MRI Dynamic Enhancement Quantitative Parameters In Distinguishing UIP And NSIP

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Research Article

Keywords: pneumonia, pulmonary, inflammation, pathological, HRCT

Posted Date: June 2nd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-533395/v1

Abstract

Background Interstitial pneumonia is a lung disease characterized by pulmonary interstitial inflammation and progressive pulmonary fibrosis. There are many causes of it, which lead to different types with different prognosis. Moreover, the mixture of different classifications will make the diagnosis difficult for radiologists, and it will also make treatment difficult for clinicians. Therefore, patients and clinicians urgently need new imaging methods to solve this problem. Currently, the most common types of interstitial pneumonia are usual interstitial pneumonia (UIP) and non-specific interstitial pneumonia (NSIP).The purpose of this article is to introduce the value of MRI dynamic enhancement quantitative parameters in the identification of UIP and NSIP.

Methods All patients with interstitial pneumonia whose images on HRCT were consistent with UIP and patients with NSIP were further examined by dynamic enhanced MRI. Follow-up was continued. Patients with UIP confirmed by pathology or ineffective after treatment and with imaging characteristics consistent with UIP were classified as UIP group (n=9). In addition, NSIP was confirmed pathologically, or the treatment was effective and the imaging characteristics were consistent with NSIP, which was classified as another group (n=18). All patients underwent high-resolution CT plain scan and MRI plain scan + dynamic enhancement scan. Different types of interstitial pneumonia were compared to obtain the dynamic enhancement quantitative parameter values at the pathological site or the most severe level was selected for the region of interest after clinical diagnosis. (Region of interest, ROI) delineate the obtained quantitative parameter values, and then compare the quantitative parameter values of MRI dynamic enhancement in each group.

Results The differences in dynamic enhancement quantitative parameters between the UIP and NSIP groups were statistically significant. Correspondingly, the pseudo-colour images formed by the lesions in these two groups were different. k^{trans} and iAUC values were lower in the UIP group than in the NSIP group, with p-values of 0.000 and 0.043 respectively; Kep and Ve values were not statistically different between the two groups. On the pseudo-colour map, the lesions in UIP were mainly blue - colourless, while the NSIP lesions were mainly light yellow - light blue.

Conclusions The quantitative parameters of MRI dynamic enhancement examinations are considered to be valuable in identifying UIP and NSIP.

Background

Interstitial pneumonia (IP) is a lung disease characterized by inflammation of the interstitial lung and progressive pulmonary fibrosis. It has a wide range of etiologies and its different subtypes have different prognoses. Currently, high resolution CT (HRCT) is used to differentiate between usual and nonspecific interstitial pneumonia, and the medications used for patients with interstitial pneumonia vary by pathological staging[1].

In nonspecific interstitial pneumonia, the use of HRCT for identification appears to be ineffective, so pathological biopsy is usually required for further examination, but it has been reported that pathological biopsy can lead to a series of complications and reduce the survival rate of patients[2].

This study evaluates the diagnostic value of dynamic contrast-enhanced MR imaging(DCE-MRI) quantitative parameters for UIP and NSIP and provide a guiding direction for clinical treatment.

Data And Methods

1.1 General information

Patients with interstitial pneumonia who were attended the hospital of Guilin Medical College between March 2019 and January 2020 were enrolled. Patients recruited include those who require a frozen lung biopsy during the course of treatment and those who are diagnosed with interstitial pneumonia at the end of the treatment process. Both types of patients require HRCT and DCE-MRI lung scan, but patients undergoing frozen lung biopsy need to complete the examination before performing the biopsy.

Patients who are recruited and complete the above examinations are followed up with HRCT lung scan, and the results of each case are evaluated and recorded as effective or ineffective based on the results of the HRCT lung scan. Cases were then divided into UIP or NSIP groups by imaging appearances and pathological and clinical diagnoses.

During this period, a total of 27 patients with interstitial pneumonia were prospectively recruited, including 9 patients (4 males and 5 females) in the UIP group, aged 45-71 years, with a median age of 58 years; 18 patients (8 males and 10 females) in the NSIP group, aged 35-73 years, with a median age of 57 years. Informed consent was obtained from all the patients and the study had been approved by the ethics committee of our institution.

Patient selection criteria: all patients with interstitial pneumonia.

Exclusion criteria for patients: 1. No pathological results and no clinical diagnosis type. 2. Pathologically and clinically diagnosed non-UIP and non-NSIP patients.

1.2 CT scan protocol

A GE light VCT 64-row, GE Optima600 128-row, or GE Revolution 256-row CT scanner was used, and CT scan was performed in all cases.There were no special requirements before the examination, and the scan was performed from the apical part of both lungs to a line 2 cm below the parallel line of the diaphragmatic angle of both ribs.

Scanning conditions: 128KV, auto milliamp, noise index 8, layer thickness and layer spacing of 5mm, using the chest algorithm to split the thin reorganization, reorganization of the layer distance and layer spacing are 1.25mm.

1.3 MRI scan protocol

1.Intravenous catheters were inserted in right elbow.

2.Equipment and scanning sequences:

SIEMENS Verio 3.0 T, 8-channel phased-array abdominal coil. Breath-hold training is performed before the examination to avoid motion artifacts that limit observation. Depending on the patient's respiratory condition, the scan time of the sequence is adjusted accordingly.

After routine scan completed, DCE-MRI of the lung was acquired with reference to the sequence provided by Siemens using the T1 VIBE technique with TE=1.66, TR=5.08, matrix=72×192, FOV=380×380mm, and layer thickness of 3.6mm. Two sequences were first scan with inversion angles of 5°and 15°under autonomic breathing, and then 35 consecutive scans were made with the sequence of inversion angle 15°, each set of 9.3 seconds, for a total of 5 minutes and 26 seconds. At the start of the 3rd scan, a dynamic bolus of gadoterate meglumine (Gd-DOTA) was administered at 0.2 mmol/kg body weight via by power injector at 2 mL/s followed by a 20 mL saline fush.

1.4 Image Analysis

Two associate-senior or higher physicians made a double-blind assessment of the HRCT images of all patients selected for the study, and the consistency was $P<0.05$.

1.5 DCE-MRI pseudo-color map and region of interest selection

The images were processed using Tissue 4D post-processing software in a syngo workstation provided by Siemens. For patients with pathologically confirmed diagnosis, the ROI(region of interest) was selected on the dynamic enhancement maps in the corresponding area and avoid proximity to the pleural, while for clinically confirmed patients, the ROI was selected on the most obvious level of the patient's lung lesion again avoiding as close to the pleural area as possible.

1.6 Statistical analysis

The SPSS 25.0 statistical software was used to perform independent t-tests for the dynamic enhancement quantitative parameters in the UIP and NSIP groups, and statistical signifcance was set at $p<0.05$.

Results

All patients successfully completed HRCT and DCE-MRI with clear images. there were statistically significant differences in the values of K^{trans} and iAUC between UIP and NSIP patients, and the K^{trans} and iAUC values of UIP patients were lower than those of NSIP ($P<0.05$) (see Table 1). On dynamic

enhancement pseudocolor images, the ROI of UIP lesions mainly showed blue-no color （Fig.1-4）, whereas the ROI of NSIP-type lesions showed mainly light yellow-light blue color （Fig.5-8）

Table 1 Comparison of quantitative parameters of UIP type and NSIP type and independent sample t-test P values

Groups	K^{trans}	K_{ep}	V_e	iAUC
UIP	0.0939±0.0272	0.9485±0.9359	0.4657±0.4936	16.0709±7.0965
NSIP	0.1671±0.0507	1.1792±1.0074	0.2694±0.0976	21.5583±0.0633
P value	0.000	0.561	0.244	0.043

HRCT map and MRI dynamic enhancement ROI delineation and pseudo color map of UIP type patients

58-year-old female with UIP. patient with UIP showed mainly linear strengthening or patchy slightly strengthening with low K^{trans}, iAUC values and mainly blue color on pseudo color map, ROI was selected at the maximum level while pseudo color map selection included lesion, healthy lung and muscle.

HRCT map and MRI dynamic enhancement ROI delineation and pseudo color map of NSIP type patients

A 53-year-old female with NSIP. the ROI was selected at the largest level of the lesion, while the pseudo-color map was selected to include the lesion, healthy lung and muscle. the NSIP patient showed mainly patchy enhancement with high K^{trans} and iAUC values relative to the UIP values and mainly blue-yellow color on the pseudo-color map.

Discussion

Interstitial pneumonia of different tissue types, mainly reflected in differences in histological types, has a different prognosis. And imaging assumes an irreplaceable task in determining pneumonia as an inflammatory or fibrotic predominant lesion [3, 4].

Patients with IP are often treated with large amounts of glucocorticoids, but this approach is not universally effective, and there are unpredictable complications if antifibrotic drugs are started immediately without identifying the type of lesion[5].Therefore, the use of non-invasive imaging methods for the early diagnosis of lung lesions in IP patients can assist physicians in selecting the right clinical treatment plan while reducing the risk of physical injury to the patient.

DCE-MRI is a functional imaging technique in which MRI is performed uninterruptedly after rapid injection of contrast agent into the patient. The contrast agent enters the extravascular space from the vascular lumen through passive diffusion, changing the signal intensity of the tissue by altering the relaxation rate of water protons, and subsequently obtaining more visual quantitative parameters and pseudo-color images by circling the area of interest.The imaging is able to quantify the blood volume, blood flow, and

vascular permeability of the lesion in the area of interest. By dynamically observing the enhancement map of the lesion area and the quantitative parameters, the blood flow and microvascular condition of the lesion can be assessed more accurately and dynamically.

The quantitative parameters are obtained by complex calculations based on DCE-MRI. The quantitative parameters K^{trans}, Kep, Ve, and iAUC represent the transfer rate constant, the rate constant, the EES volume fraction, and the initial area under the time-concentration curve, respectively.

They represent the following meanings: K^{trans}: the amount of contrast agent entering the extravascular extracellular space from the vessel per unit time, which is an absolute parameter of the perfusion rate and is also influenced by the tissue permeability. Kep: the contrast dose returning from the extravascular extracellular space to the vessel. Ve: the percentage of the extravascular extracellular space volume to the whole volume of the area of interest. iAUC: reflects the combined change of the above three indicators and is one of the semi-quantitative parameters.These parameters are based on the "Toft" model [6] and are divided into two zones based on the distribution of the contrast agent, the first zone being the central zone, which consists mainly of intravascular extracellular volume fraction (blood plasma), and the peripheral zone, which consists of extravascular extracellular volume fraction. The flow of contrast agent in this model is bidirectional, first flowing from the vascular lumen to the extracellular space outside the vessel, and after a period of time, contrast agent elutes back into the vasculature from the extracellular space outside the vessel. This continuous variation is well described by DCE-MRI, and the quantitative parameters are calculated by substituting the continuous image signal intensity variation into the model. On the dynamic enhancement pseudo-color map, red represents high perfusion, yellow represents slightly high perfusion, and blue represents low perfusion. So the closer the color to red, indicates the more adequate the blood supply, and the closer to blue, the poorer the blood supply.

There have been studies using DCE-MRI in the pancreas and breast [7, 8], but DCE-MRI is rarely used in interstitial pneumonia.

A total of 27 cases were enrolled in this study, including 10 cases in the UIP group and 17 cases in the NSIP group. In this study, we found that the K^{trans}, iAUC values of UIP patients were lower than those of NSIP patients.The cause of this phenomenon is the abnormal accumulation of fibroblasts and inflammatory cells occurring in the lungs of UIP patients, replacing the normal interstitial structures of the lungs and causing damage to the alveolar epithelium, which is a stress point for pulmonary fibrosis, leading to damage to the interstitial capillaries and eventually causing irreversible distortion of the alveolar structures [9].Irreversible distortion of the alveolar structure hinders the "drainage" of the contrast agent from the lesion and is accompanied by difficulty in retreating or entering the contrast agent. Eventually, the lung tissue forming the honeycombed lung has lost its blood supply or receives limited blood supply, so the K^{trans}, iAUC values are reduced, and the ROI of the UIP lesion is mainly blue-apochromatic on the corresponding dynamic enhancement pseudocolor image.

In contrast, NSIP-type lesions are mainly characterized by infiltration of inflammatory cells, widening of extravascular spaces and increased neovascularization [10], so the contrast agent enters the lesion without obstruction and elutes out of the lesion more rapidly, so the K^{trans} and iAUC values are correspondingly higher, and then the color is mainly light yellow-light blue on the dynamic enhancement pseudo-color map. Moreover, Boesen et al used DCE-MRI and found that infectious osteoarthropathy leads to more neovascularization and increased perfusion in the lesion, which is also approximately the same as the results of the present study [11].

In conclusion, we found that quantitative parameters and dynamic enhancement pseudo-color maps have diagnostic significance in assessing IP, among which K^{trans} and iAUC values of quantitative parameters have discriminatory significance in identifying UIP and NSIP, with K^{trans} value as the greatest diagnostic efficacy. However, the sample size of this study is still small, and it is necessary to further expand the sample size to accurately identify the quantitative parameters of UIP and NSIP.

Abbreviations

UIP：usual interstitial pneumonia

NSIP：non-specific interstitial pneumonia

DCE-MRI：dynamic contrast-enhanced MR imaging

Declarations

Ethics approval and consent to participate

The study was approved by the patient's：age>18： informed consent and the study was approved by the ethical review of the Affiliated Hospital of Guilin Medical College.All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analyzed in this study are available from the corresponding author on request.

Competing interests

The authors declare that they have no competing interests.

Funding

Guangxi Key Laboratory of Molecular Medicine in Liver Injury and Repair(GXLIRMMKL-K202010).

Acknowledgments

I sincerely thank all the authors for their efforts in this article

Authors' contributions

Xinhui Chen, Ge Cheng and Zhipeng Zhou conceived and designed this study. Xinhui Chen and xinguan Yang conducted the study and collected important background data. Yufang Hu is responsible for the chest MRI scan of the patient. Xinhui Chen drafted the manuscript. All authors read and approved the final manuscript.

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References

[1] Fragoulis GE, Nikiphorou E, Larsen J, et al. Methotrexate-Associated Pneumonitis and Rheumatoid Arthritis-Interstitial Lung Disease: Current Concepts for the Diagnosis and Treatment. Front Med(Lausanne), 2019, 6:238.

[2] Hutchinson JP, Fogarty AW, McKeever TM, et al. In-Hospital Mortality after Surgical Lung Biopsy for Interstitial Lung Disease in the United States. 2000 to 2011. Am J Respir Crit Care Med. 2016, 193(10):1161-1167.

[3] Puglisi S, Torrisi SE, Giuliano R, et al. What We Know About the Pathogenesis of Idiopathic Pulmonary Fibrosis. Semin Respir Care Med, 2016, 37(3):358-67.

[4] Nicholson A, Colby T, Dubois R, et al. The Prognostic Significance of the Histologic Pattern of Interstitial Pneumonia in Patients Presenting with the Clinical Entity of Cryptogenic Fibrosing Alveolitis. Am J Respir Crit Crit Care Med, 2000, 162(6):2213-2217.

[5] Valenzuela C, Torrisi SE, Kahn N, et al. Ongoing challenges in pulmonary fibrosis and insights from the nintedanib clinical programme.Respir Res. 2020, 21(1):7.

[6] Gaddikeri S, Gaddikeri RS, Tailor T, et al. Dynamic Contrast-Enhanced MR Imaging in Head and Neck Cancer: Techniques and Clinical Applications. AJNR Am J Neuroradiol. 2016, 37(4):588-95.

[7] Tang W, Liu W, Li HM, et al. Quantitative dynamic contrast-enhanced MR imaging for the preliminary prediction of the response to gemcitabine-based chemotherapy in advanced pancreatic ductal carcinoma. Eur J Radiol. 2019 Dec;121:108734. doi: 10.1016/j.ejrad.2019.108734.

[8] Jun W, Cong W, Xianxin X, et al. Meta-Analysis of Quantitative Dynamic Contrast-Enhanced MRI for the Assessment of Neoadjuvant Chemotherapy in Breast Cancer. Am Surg. 2019, 85(6):645-653.

[9] Bagnato G, Harari S. Cellular interactions in the pathogenesis of interstitial lung diseases. Eur Respir Rev, 2015, 24(135):102-114.

[10] Tzouvelekis A, Anevlavis S, Bouros D. Angiogenesis in Interstitial Lung Diseases: a pathogenetic hallmark or a bystander?. Respir Res Respiratory Research, 2006, 7(1):82-94.

[11] Boesen M, Kubassova O, Sudoł-Szopińska I, Maas M, et al. MR Imaging of Joint Infection and Inflammation with Emphasis on Dynamic Contrast-Enhanced MR Imaging. PET Clin. 2018, 13(4):523-550.

Figures

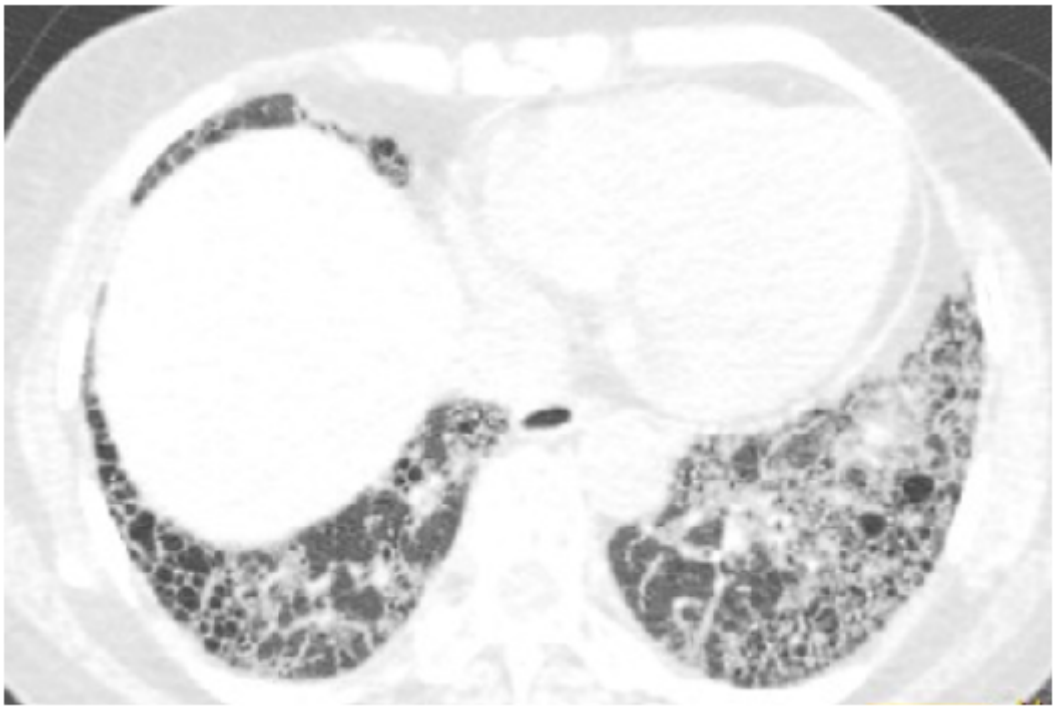

Figure 1

HRCT map

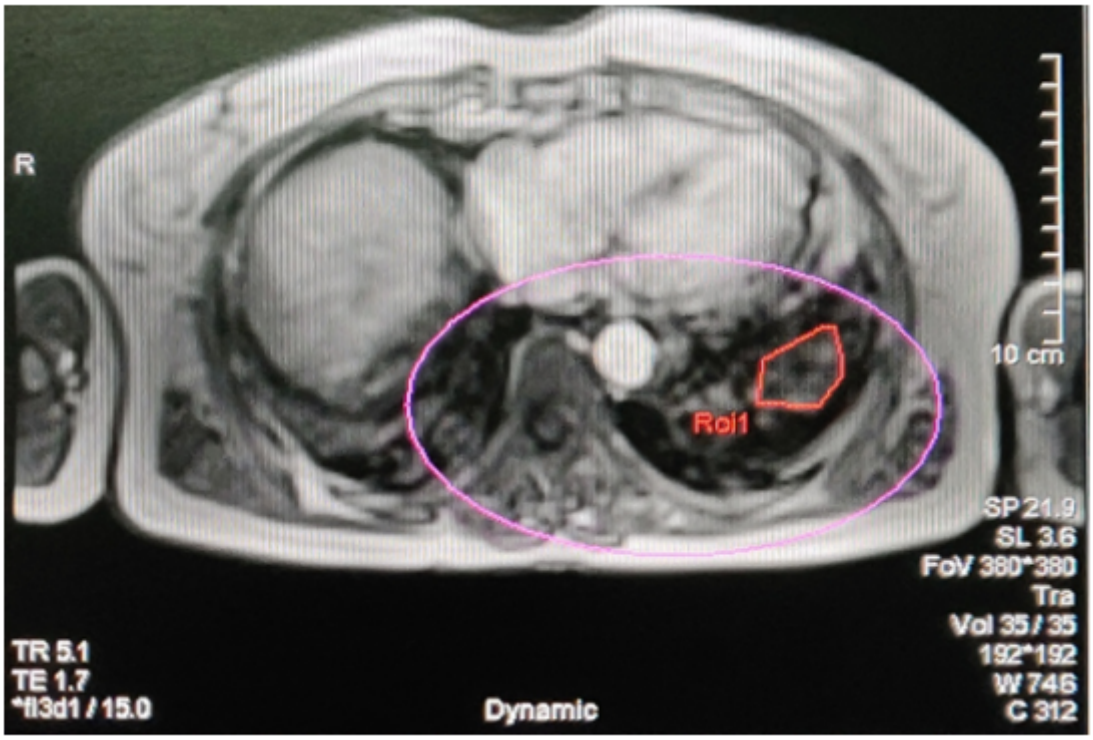

Figure 2

MRI dynamic enhancement ROI delineation and pseudo color map of UIP type patients

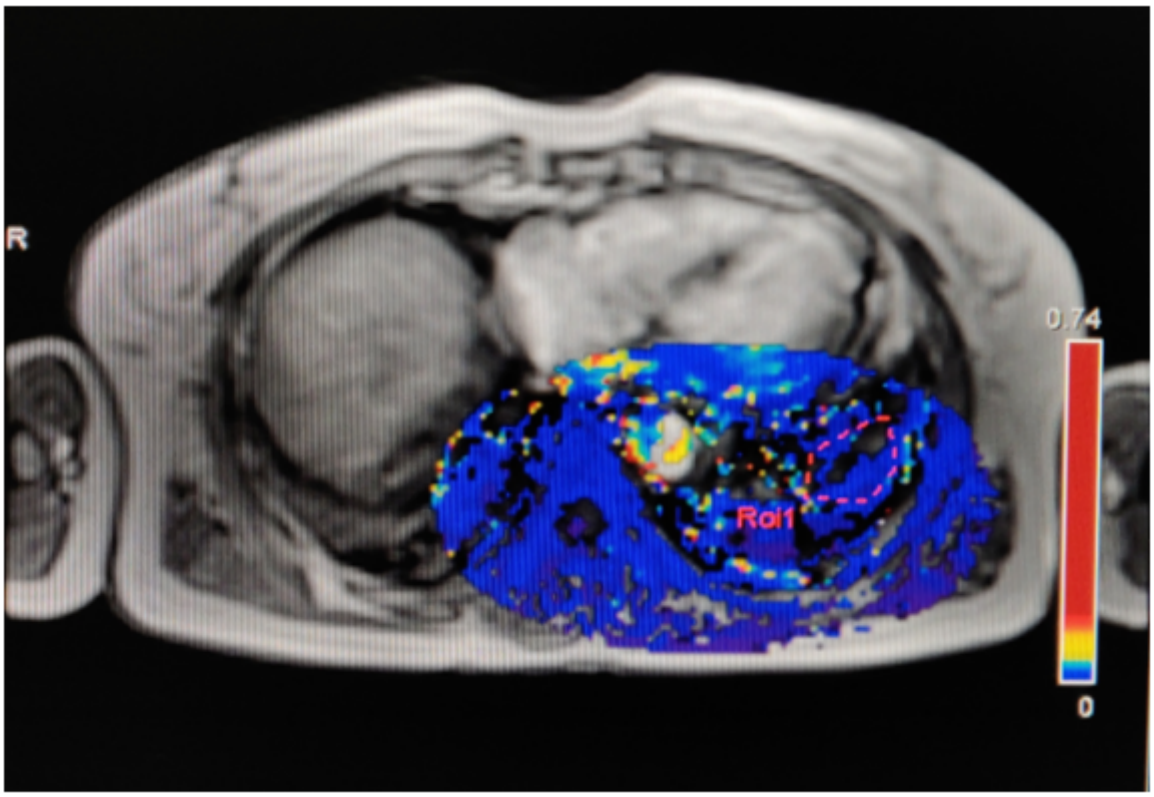

Figure 3

58-year-old female with UIP.

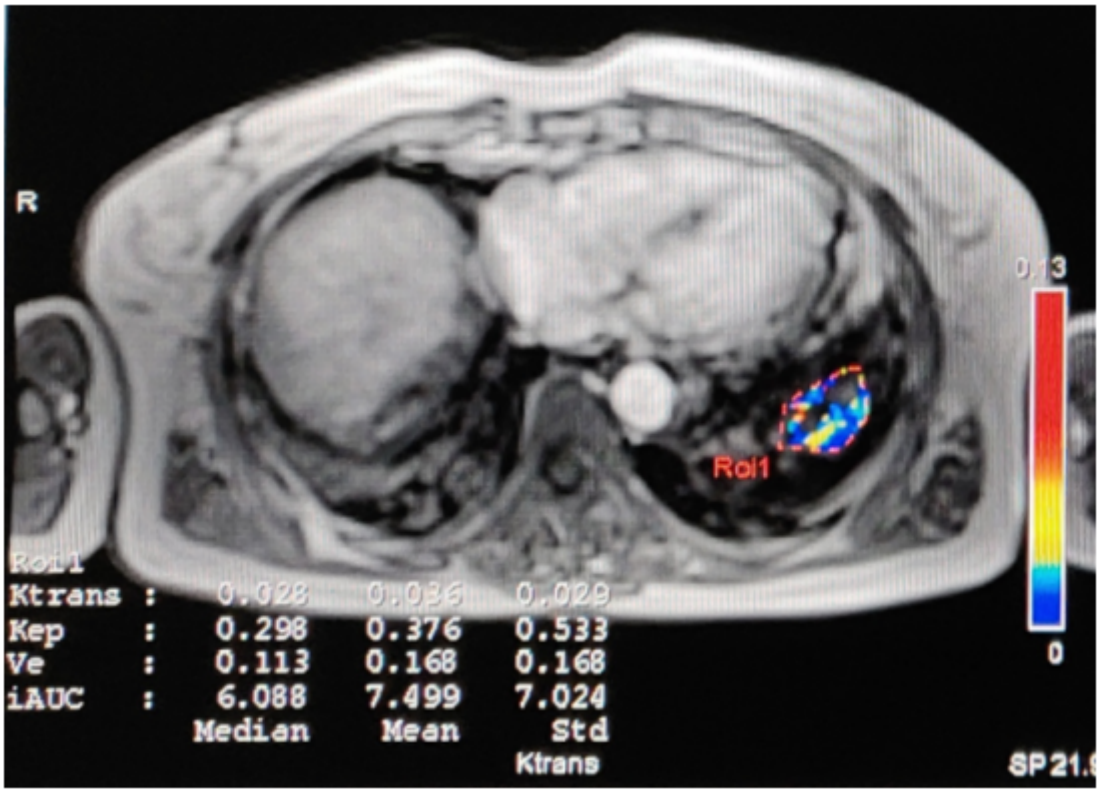

Figure 4

Patient with UIP showed mainly linear strengthening or patchy slightly strengthening with low Ktrans, iAUC values and mainly blue color on pseudo color map

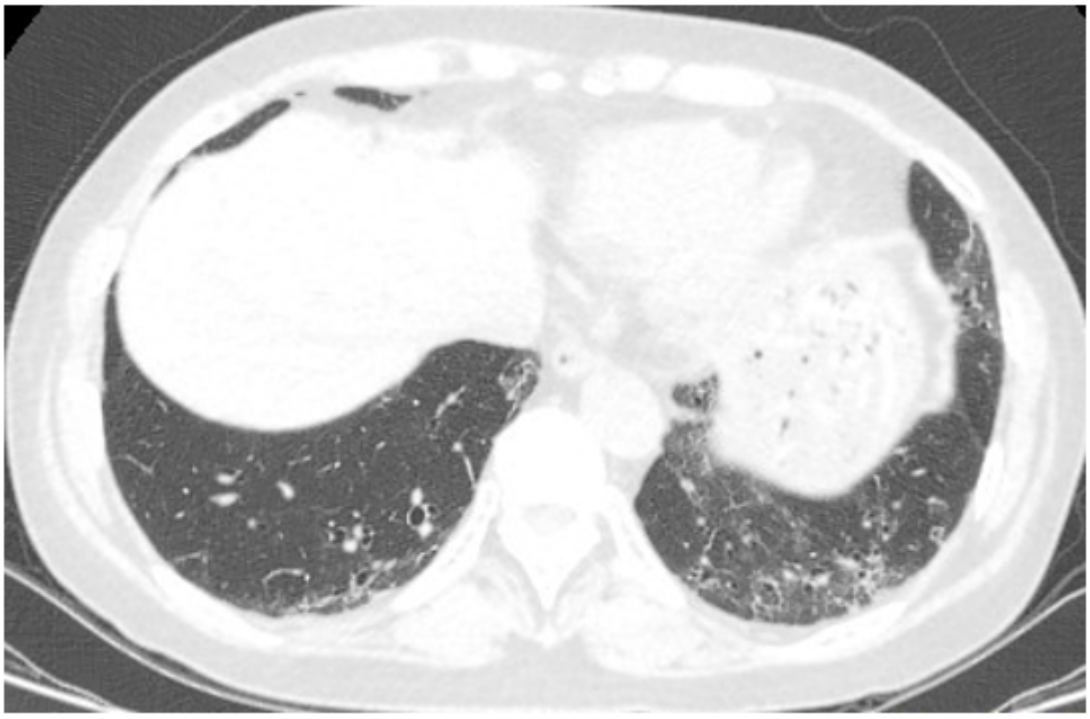

Figure 5

HRCT map

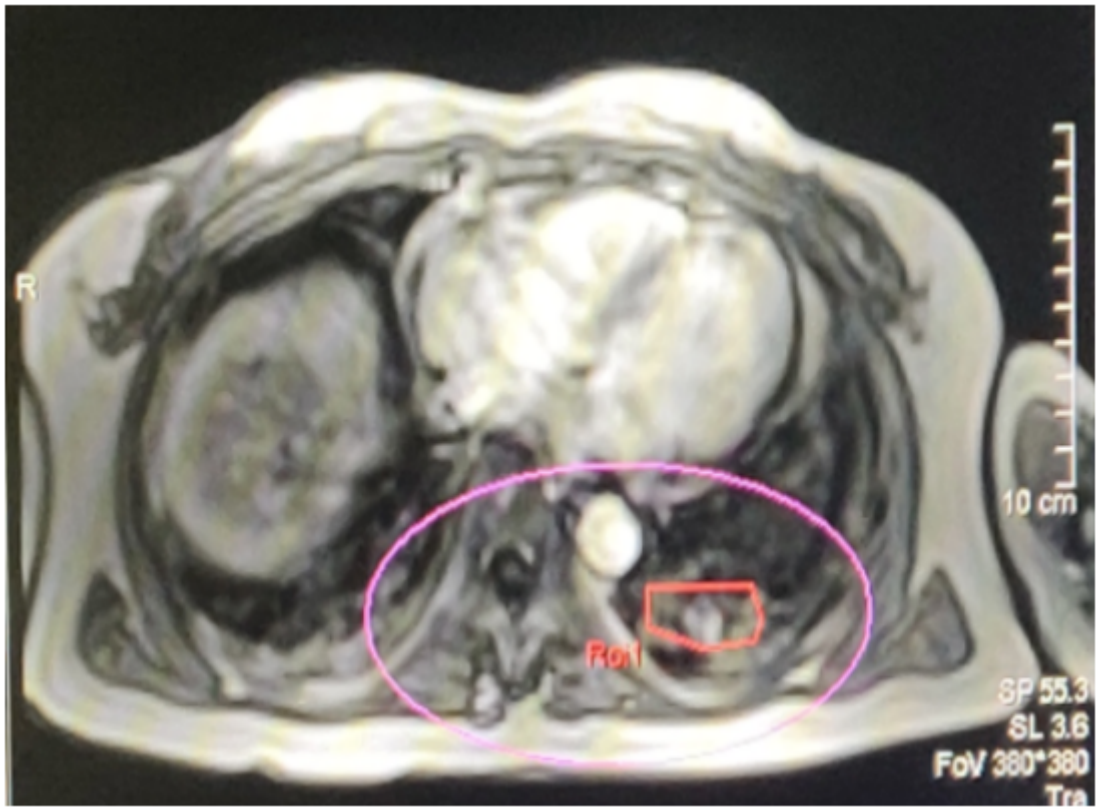

Figure 6

MRI dynamic enhancement ROI delineation and pseudo color map of NSIP type patients

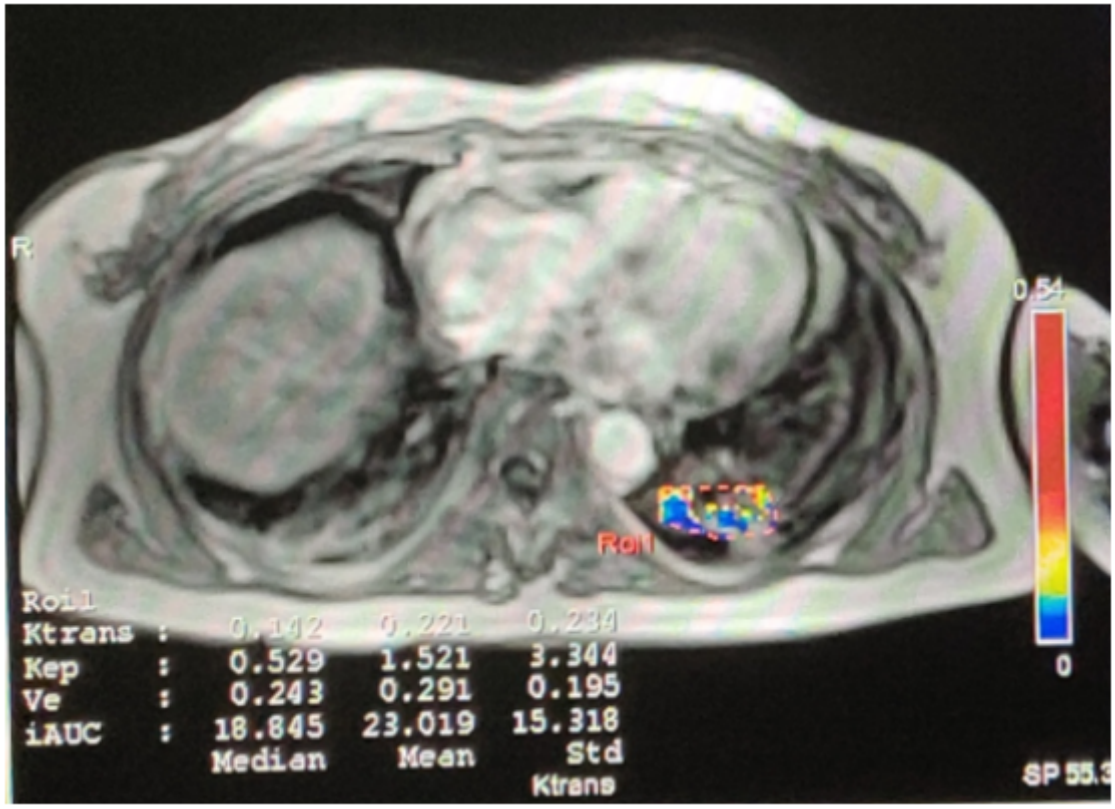

Figure 7

A 53-year-old female with NSIP. the ROI was selected at the largest level of the lesion, while the pseudo-color map was selected to include the lesion, healthy lung and muscle.

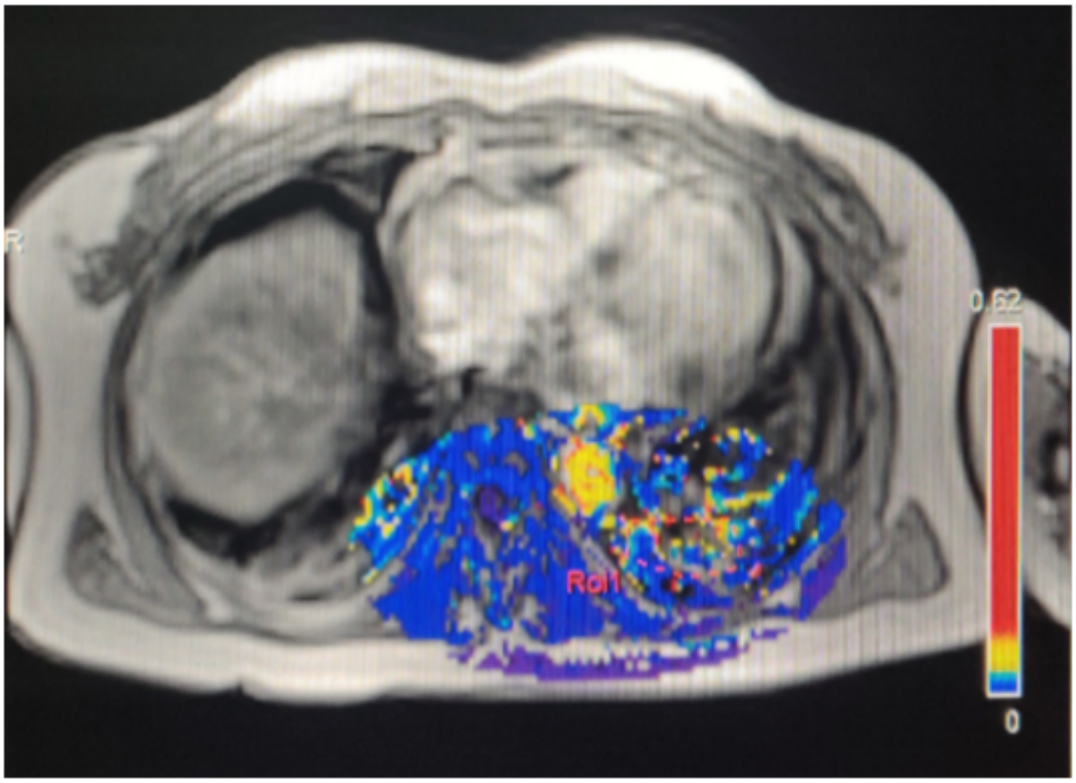

Figure 8

The NSIP patient showed mainly patchy enhancement with high Ktrans and iAUC values relative to the UIP values and mainly blue-yellow color on the pseudo-color map.