Reproducibility study on quantitative ultrasound shear wave viscoelastography for diffuse liver disease

Sathiyamoorthy Selladurai[1], Manish Bhatt[1], Ladan Yazdani[1], Iman Rafati[1], Francois Destrempes[1], Boris Chayer[1], Marie-Helon Roy Cardinal[1], Francois Yu[1], Marc Gesnik[2], Emmanuel Montagnon[3], Miloud Zentai[3], Barat Maxim[3], An Tang[3], Guy Cloutier[1,3,4]

[1]Laboratory of Biorheology and Medical Ultrasonics (LBUM), University of Montreal Hospital Research Center (CRCHUM), Montréal, QC, Canada; University of Montreal, Montréal, QC, Canada;

[2]ICONEUS, Paris, France

[3]Laboratory of Clinical Image Processing, CRCHUM, Montréal, QC, Canada; Department of Radiology, University of Montreal Hospital, Montréal, QC, Canada; and Department of Radiology, Radiation Oncology, and Nuclear Medicine, University of Montreal, Montréal, QC, Canada

[4]Institute of Biomedical Engineering, University of Montreal, Montréal, QC, Canada

Université de Montréal

LBUM

CRCHUM
CENTRE DE RECHERCHE
Centre hospitalier de l'Université de Montréal

Cancer Research Society

SIEMENS

INSTITUT TRANSMEDTECH MONTRÉAL

MEDTEQ
L'INNOVATION POUR LA SANTÉ
INNOVATION FOR HEALTH

Département de radiologie, radio-oncologie et médecine nucléaire
Faculté de médecine
Université de Montréal

Disclosures

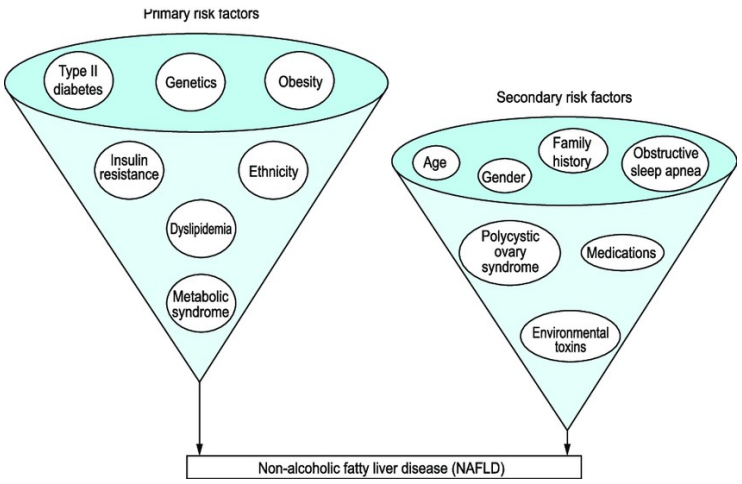
N/A

Département de radiologie, radio-oncologie
et médecine nucléaire
Faculté de médecine
Université de Montréal

Introduction

Non Alcoholic Fatty Liver Disease(NAFLD)

Risk factors



Prevalence

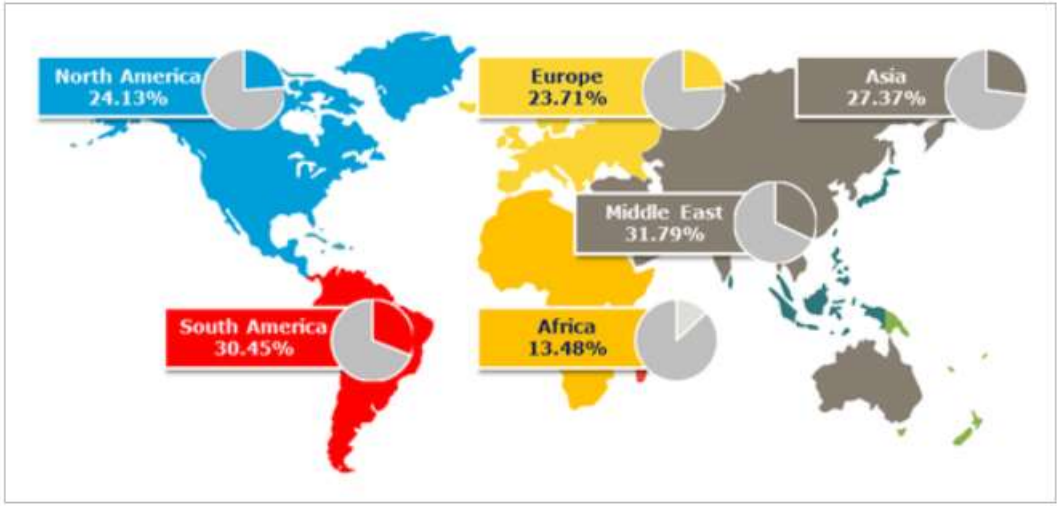


Fig.1.Non-alcoholic fatty liver disease a) Risk factors , b)prevalence rates reported from Asia, Europe, Middle East, North America and South America

In humans, the natural history leading from nonalcoholic fatty liver disease (NAFLD) to nonalcoholic steatohepatitis (NASH) is not completely understood; hence, there is a need to improve the noninvasive characterization of the fatty liver disease spectrum to improve diagnosis and prognosis of NAFLD.

- NAFLD is rapidly becoming the most common liver disease worldwide .

Courtesy: S.K. Sarin et al.,

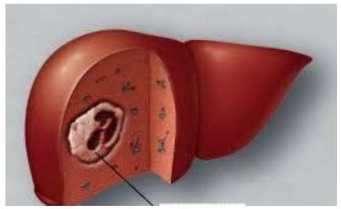
1. Younossi, Zobair, et al. "Global perspectives on nonalcoholic fatty liver disease and nonalcoholic steatohepatitis." *Hepatology* 69.6 (2019): 2672-2682.

Département de radiologie, radio-oncologie et médecine nucléaire
Faculté de médecine
Université de Montréal

Introduction: Liver disease

Diffuse liver disease

Liver tumor



•Diffuse or focal modification of liver stiffness due to fibrosis, Liver mass, Vascular congestion, inflammation, cholestasis.

• Accurate assessment of the degree of liver fibrosis is important for estimating prognosis and deciding on an appropriate course of treatment for cases of liver disease.(WK Jeong,2014).

• As diseases stage increases, **changes in tissue stiffness** occurs (N. Frulio-2013).

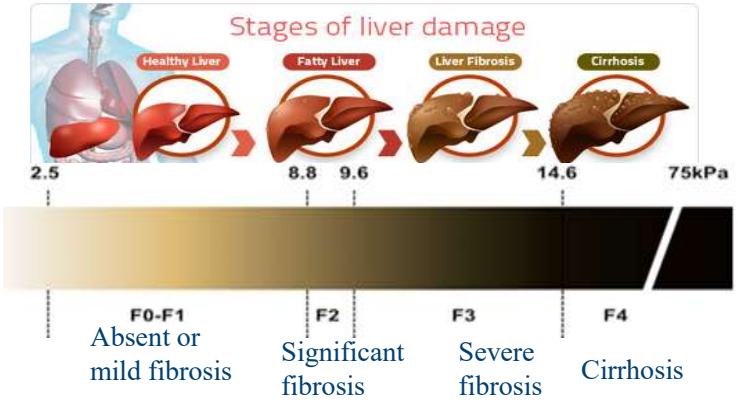


Fig.2: The stages of liver disease classification using current clinical markers and its correlation with young's modulus are shown here.

Courtesy: Francesco Paparo et al.,

Liver biopsy

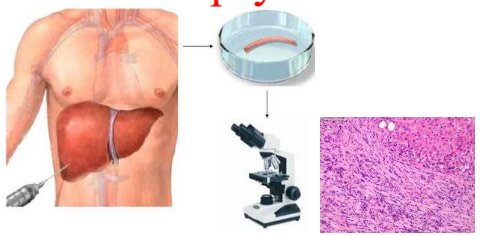


Fig. 3: For diagnosis of liver fibrosis, biopsy is still considered as the gold standard method and widely used in clinical practice

- Invasiveness
- Physical and mental discomfort to the patient.
- Very small size of samples obtained through biopsy may not represent a disease condition .
- Not suitable for treatment follow-up
- Sampling error, and Cost

Courtesy: Woo et al. 2014

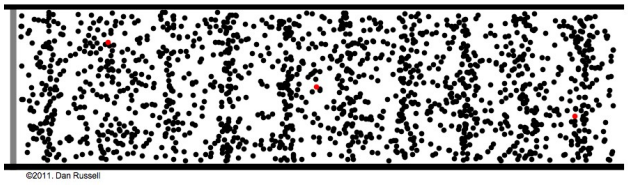
Département de radiologie, radio-oncologie et médecine nucléaire
Faculté de médecine
Université de Montréal

Introduction

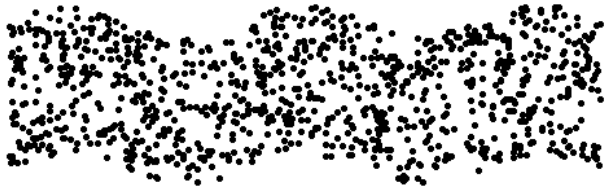
Usual imaging is done with compression waves

Any wave/deformation propagating in an (isotropic) medium can decomposed in two waves

Compression wave



Shear wave



In the biological tissues case :

- $c_p \approx 1500$ m/s

$c_s \approx 1$-5 m/s

Usual type of wave in ultrasound imaging

Used in Elastographic imaging

Most prior studies considered only stiffness as a biomarker while not exploiting the lossy nature of the liver. Thus, having more than 1 viscoelasticity biomarker could be useful to obtain more insight on liver parenchyma state.

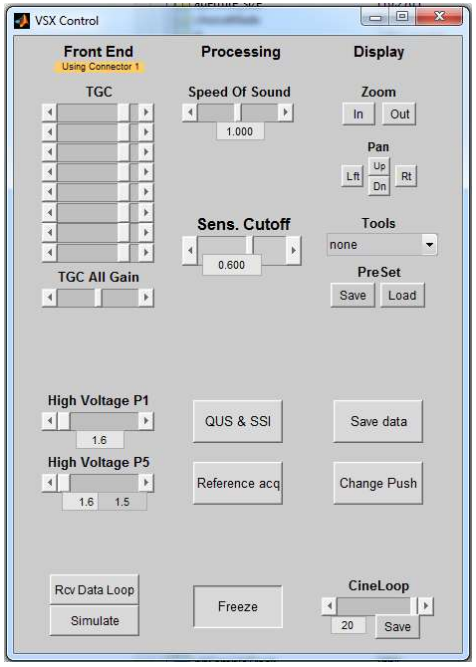
Département de radiologie, radio-oncologie et médecine nucléaire
Faculté de médecine
Université de Montréal

Methods

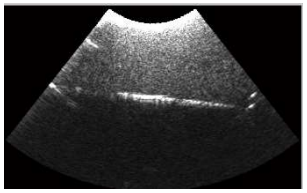
Methods

Assessed ultrasound-SW elastography parameters such as the shear-wave speed (SWS) and its dispersion, SW attenuation, Young's modulus, viscosity, and shear modulus in participants coming for 2 visits.

Furthermore, histopathology analysis (liver biopsy ground truth) was done on liver-tissue samples. We also compared US-SW elastography parameters with biopsy results.



Live B-mode



Acquisition

Shear wave mode

- Shear wave speed
- Young's Modulus Stiffness (E or μ)
- Attenuation
- Viscosity (η)
- Shear Modulus

- Verasonics = programmable research ultrasound scanner (Matlab)

Département de radiologie, radio-oncologie et médecine nucléaire
Faculté de médecine
Université de Montréal

Methods

Multi-parametric shear wave elastography

- Shear wave speed(C)
  - –Velocity field (2-D auto corrélation algorithm)(Lopas at al., 1995)
  - –ROI 1cm x 1cm 0.5mm from push location
  - –Shear Wave Speed(SWS)(Deffieux et al.,2009)
- Viscoelasticity parameters
  - –Stiffness (Young's modulus $Y = 3\rho c^2$)
  - –Viscosity ($\eta = \frac{G''}{\omega}$)
  - –Viscoelasticity ($G = G' + iG''$)
- SW Dispersion: SWS is frequency dependent measure, the dispersion was assessed as its slope vs frequency. (Barry et al. 2012; Parker et al., 2015),
- SW Attenuation(Bernard et al.,2016).
  - –Frequency shift method.

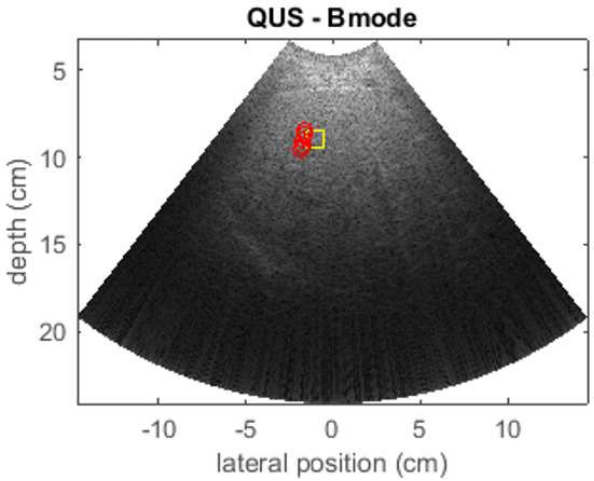
1. M. Bhatt, L. Yazdani, F. Destrempes, L. Allard, B. Nguyen, A. Tang, and G. Cloutier, "Multiparametric *in vivo* ultrasound shear wave viscoelastography on farm-raised fatty duck livers". **Poultry Science**, 100(4) ,100968, 2021.
2. M. Gesnik, M. Bhatt, M.H. Roy-Cardinal, F. Destrempes, L. Allard, B. N. Nguyen, T. Alquier, J.F. Giroux, A. Tang, and G. Cloutier, "*In vivo* ultrafast quantitative ultrasound and shear wave elastography imaging on farm-raised duck livers during force feeding". **Ultrasound in Medicine and Biology**, 46(7), 1715-1726, 2020.
3. S. Bernard, S. Kazemirad and G. Cloutier, "A Frequency-Shift Method to Measure Shear-Wave Attenuation in Soft Tissues," in IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control, vol. 64, no. 3, pp. 514-524, March 2017, doi: 10.1109/TUFFC.2016.2634329.

Département de radiologie, radio-oncologie et médecine nucléaire
Faculté de médecine
Université de Montréal

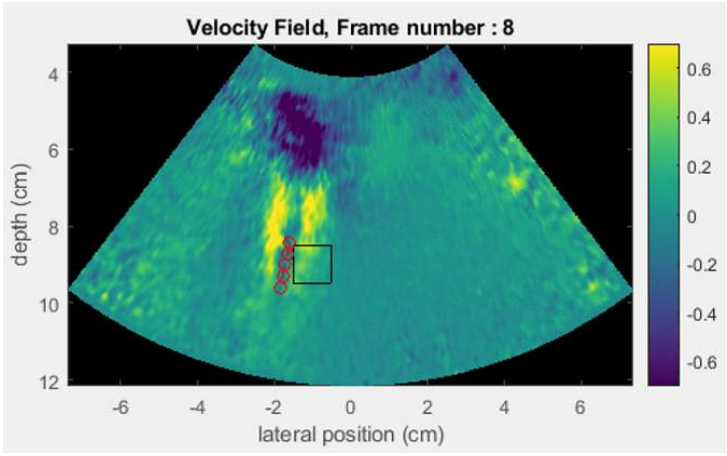
Results

Patient 1, Visit 1

A)



B)



C)

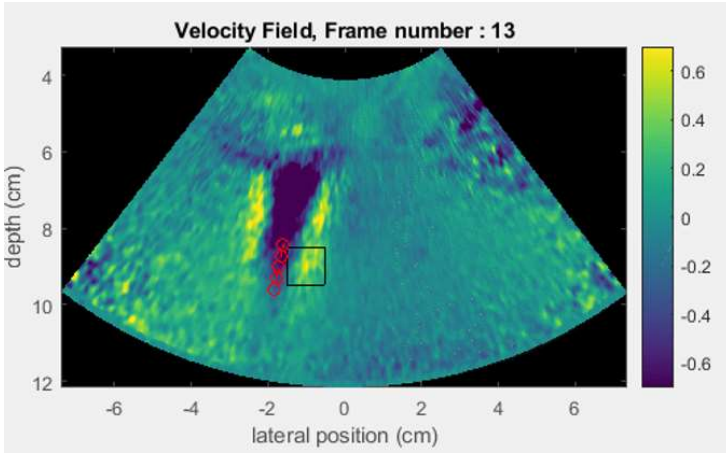
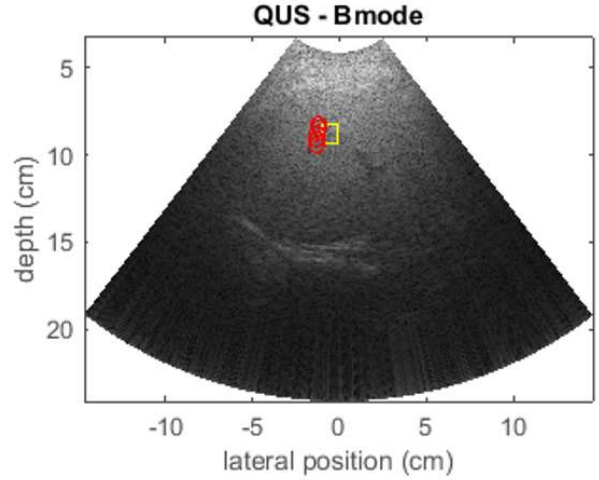


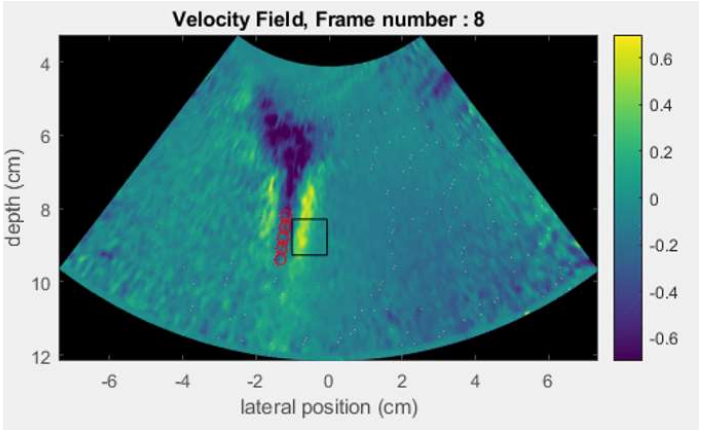
Figure 4 shows Patient 1, Visit 1, A) a B-mode image of a NASH patient, B&C) the SW velocity field, where the red-circle indicates the SW push location, and the yellow-square ROI measurements made next to the SW push.

Patient 1, Visit 2

A)



B)



C)

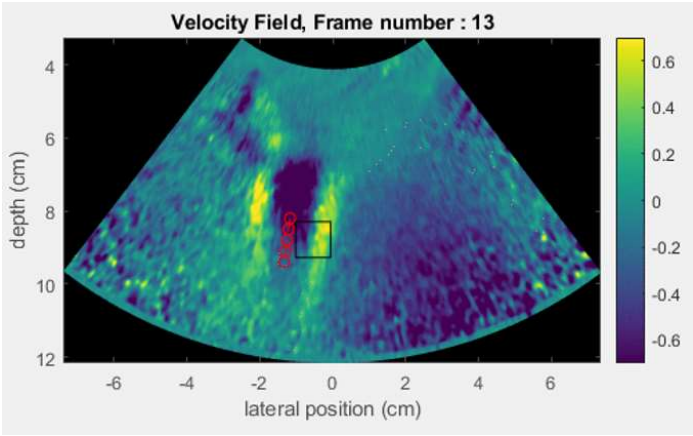


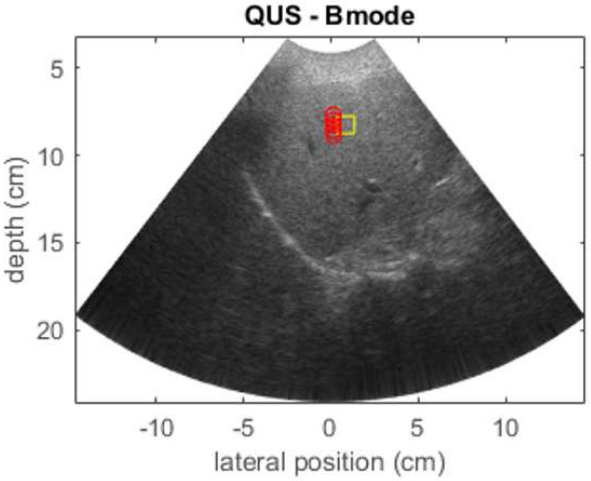
Figure 5 shows Patient 1, visit 2, A) a B-mode image of a NASH patient, B&C) the SW velocity field, where the red-circle indicates the SW push location, and the yellow-square ROI measurements made next to the SW push.

Département de radiologie, radio-oncologie et médecine nucléaire
Faculté de médecine
Université de Montréal

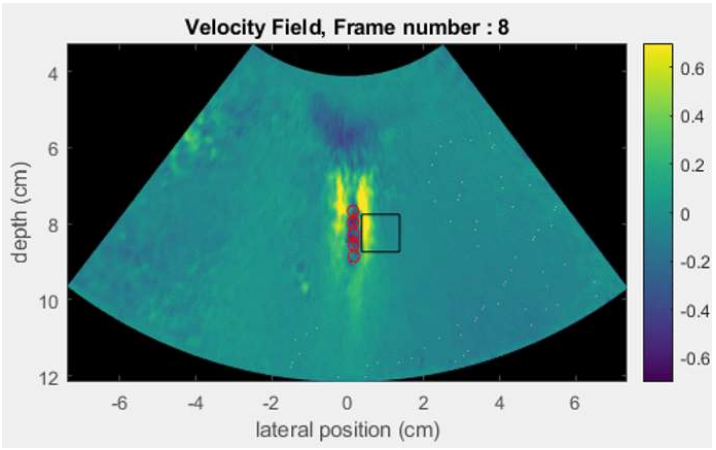
Results

Patient 1, Visit 1

A)



B)



C)

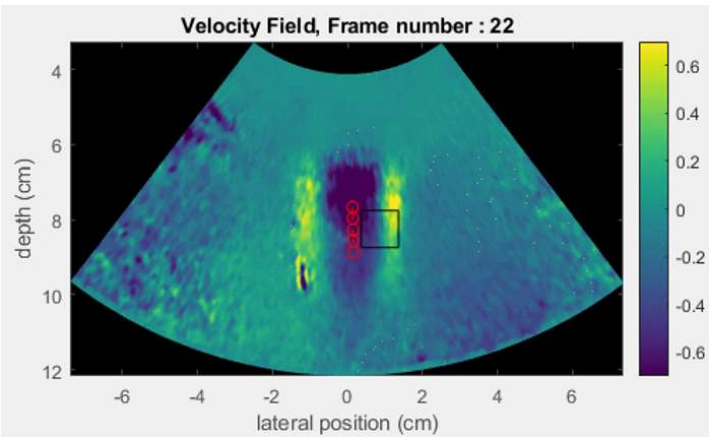
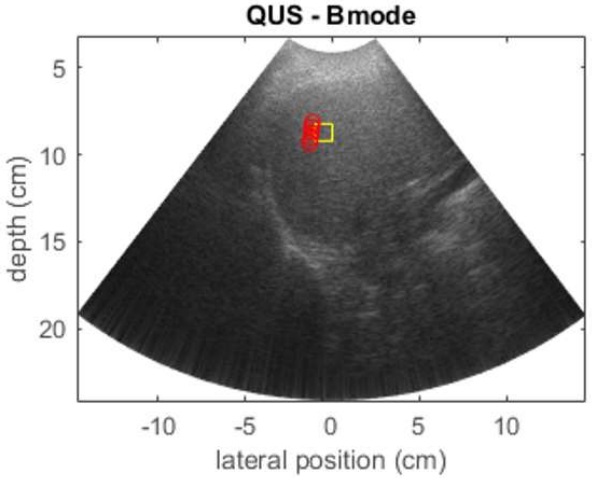


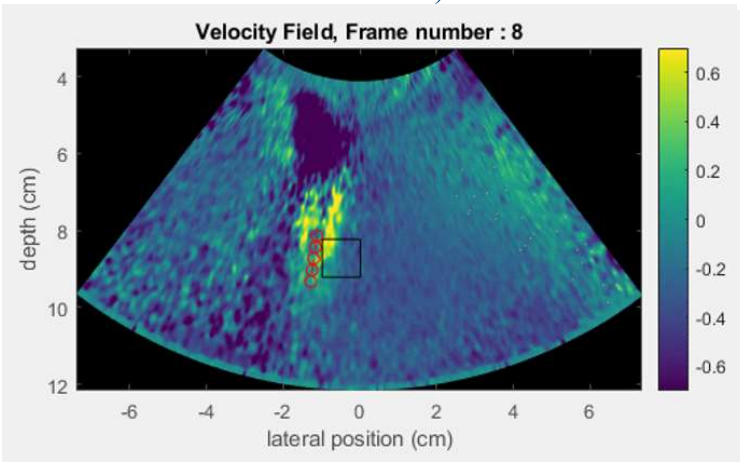
Figure 5 shows Patient 2, Visit 1, A) a B-mode image of a NASH patient, B&C) the SW velocity field, where the red-circle indicates the SW push location, and the yellow-square ROI measurements made next to the SW push.

Patient 1, Visit 2

A)



B)



C)

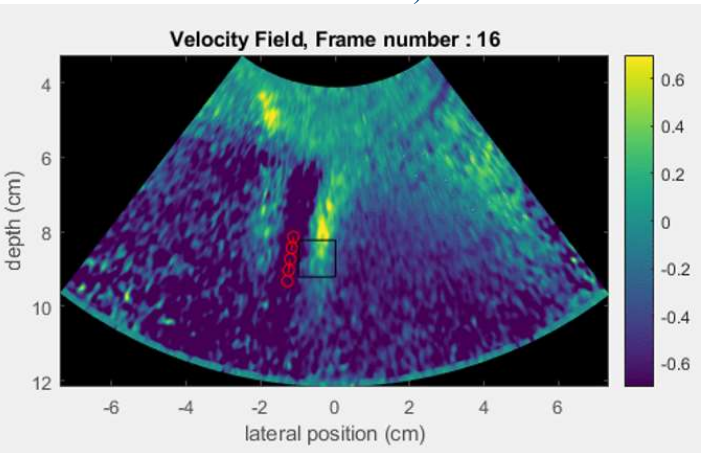
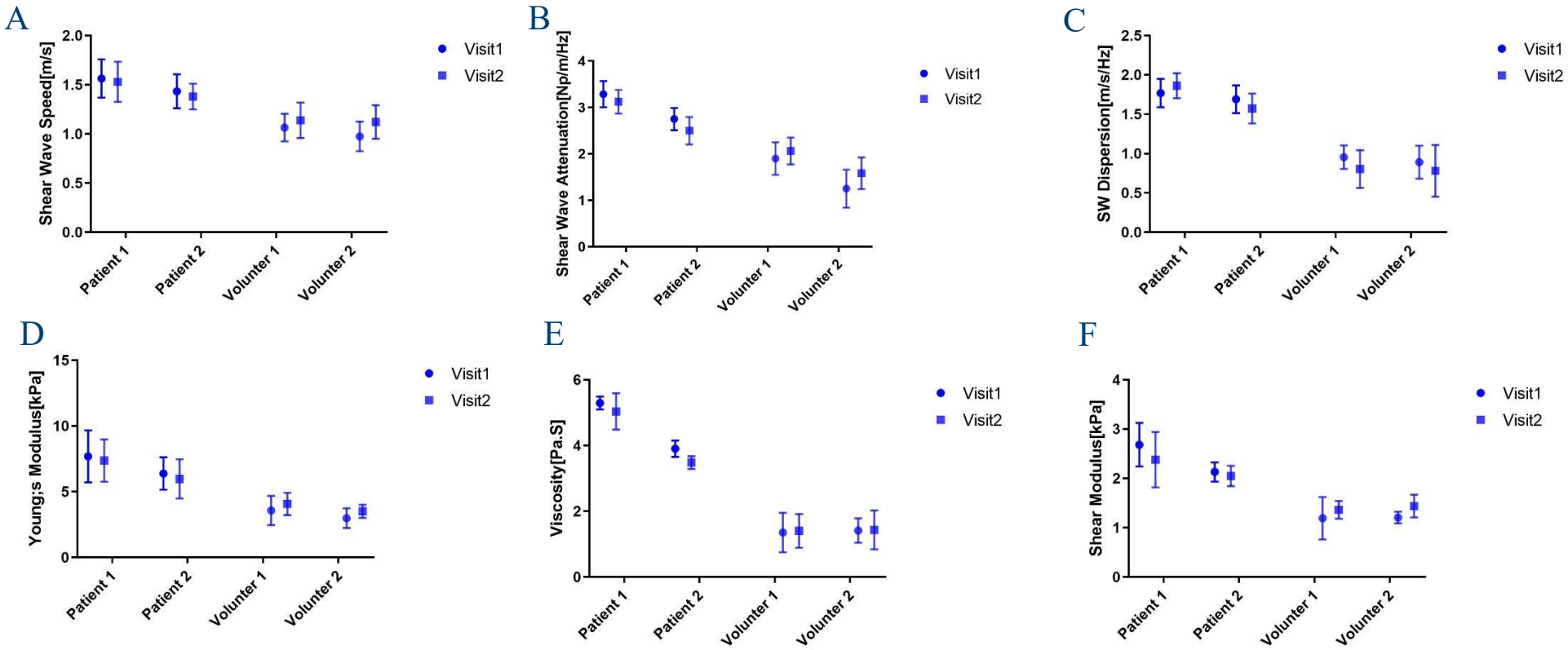


Figure 6 shows Patient 2, visit 2, A) a B-mode image of a NASH patient, B&C) the SW velocity field, where the red-circle indicates the SW push location, and the yellow-square ROI measurements made next to the SW push.

Département de radiologie, radio-oncologie et médecine nucléaire
Faculté de médecine
Université de Montréal

Results and Conclusions



Results: Figure 7 shows measurements (mean±SD, n=10) observed in NASH patients and volunteers: A) SW speed, B) SW attenuation, C) SW speed dispersion, D) Young's modulus, E) viscosity , and F) shear modulus.

Patients 1 &2 were staged as F2-fibrosis using biopsy. The US-SW results show that measurements are reproducible between the two visits.

Conclusions: Having more than one viscoelasticity biomarker could be useful to obtain more insight on NASH disease**.** Reproducibility (NASH dataset visits-1 and 2) seems acceptable for clinical assessment of the method on a larger dataset**.** This methodology may be used for diagnosis and treatment follow-up in diffuse liver disease.

Département de radiologie, radio-oncologie
et médecine nucléaire
Faculté de médecine
Université de Montréal