Title:

Noninvasive diagnosis of lesions in homogenous media using a regularized phantom-free construction of local attenuation coefficient slope maps

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Date:

3rd February 2022

Location:

Virtual Seminar 2022

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et médecine nucléaire
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Disclosures

Technical developments were supported by the Onco-Tech program jointly funded by the Fonds de Recherche Santé du Québec, Oncopole, Medteq, TransMedTech, Cancer Research Society, and Siemens Healthcare. This program is continued through the support of the Natural Sciences and Engineering Research Council of Canada (Alliance program in partnership with Siemens Healthcare).

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1. Introduction

Serious situation (Worldwide)

- Hepatocellular carcinoma (HCC) is responsible for approximately 90% of primary hepatic cancer cases [1].
- HCC is one of the most prevalent cancer worldwide [2].
- The mortality rate of HCC is increasing 3% per year due to the late diagnosis of this cancer [3].

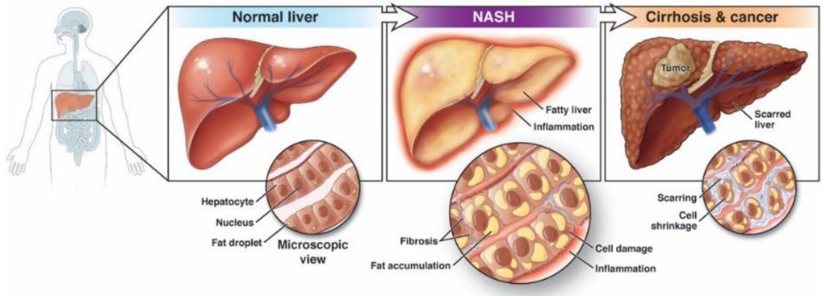

Image Ref: https://gastro.org/practice-guidance/gi-patient-center/topic/nonalcoholic-steatohepatitis-nash/

Problems and treatment methods

- ✓ There is an urgent need to improve early detection of HCC.
- ✓ Surveillance with Ultrasound (US) is an cost effective option but US suffer from low accuracy.
- ✓ Improving US characterization would provide new cost-effective and safe strategies for patient management, compared to MRI, CT or biopsy.

Improving US and Objective

- ✓ Calculating some parameter such as US **Attenuation** can improve the detection using US.
- ✓ Attenuation can be considered as an imaging **artifact** or, on the contrary, as a specific feature with **diagnostic value.**
- ✓ **Attenuation maps** based on local attenuation coefficient slope (ACS) in quantitative ultrasound (QUS) have shown potential for diagnosis of steatotic and cancerous livers. We considered the construction of semantic parametric maps and an approach providing a phantom-free (PF) estimation of local ACS. **The main goal was to propose a methodology for constructing regularized PF local ACS maps, and investigate the performance in homogeneous media with inclusions.**
- ✓ The proposed method, on the contrary to conventional methods ,does not need to have an acquisition from reference phantom each time which is not convenient to clinician.

[1] J. M. Llovet *et al.*, "Hepatocellular carcinoma," *Nature Reviews Disease Primers,* 2021.
[2] W. Wang and C. Wei, "Advances in the early diagnosis of hepatocellular carcinoma," (in eng), *Genes Dis,* 2020.
[3] K. A. Cronin *et al.*, "Annual Report to the Nation on the Status of Cancer, part I: National cancer statistics," (in eng), *Cancer,* 2018.

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2. Method

2.1 Theory summary

Phantom free method (PF)

Modifications brought to [1] previous works include:

a. a linear interpolation of the power spectrum in log-scale;
b. the relaxation of the underlying hypothesis on the diffraction factor;
c. a generalization to nonhomogeneous local ACS; and
d. an adaptive restriction of frequencies to a more reliable range for this purpose than the usable frequency range.

As in [2,3], regularization was formulated as generalized LASSO [4], and the variant of the Bayesian Information Criterion (BIC) [5] introduced in [2,3] was applied to estimate the Lagrangian multiplier on the LASSO constraint.

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We compared results with the spectral log difference (SLD) method requiring a calibration phantom, and to the planar reflection technique used as a ground truth in experimental phantoms

[1] Gong P et al (2019) *IEEE TUFFC* 6: 867-875.
[2] Rafati et al (2020) *IEEE IUS*
[3] Destrempes et al (2019) *IEEE IUS*: 2027-2030.
[4] Tibshirani RJ et al (2011) *Ann Stat* 39: 1335-1371.
[5] Schwartz G (1978) *Ann Stat* 6: 461-464

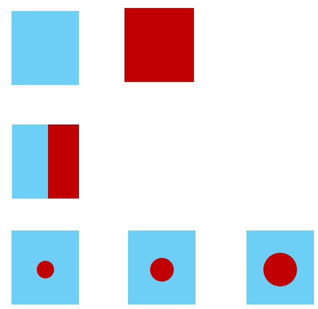
2. Method

2.2 Phantom fabrication

Homogeneous phantoms

Side-by-side phantoms

Inclusion phantoms



Diameter: 10mm 15mm 20 mm

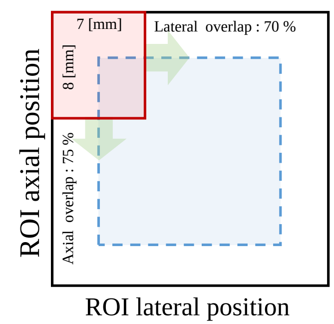
	mixture #1	mixture #2
agar	2%	2%
glycerol	10%	10%
graphite powder	4.5%	12%

2.3 Experiment descriptions

- Ultrasound acquisitions were performed with a Verasonics Vantage 256 scanner (Redmond, WA) using an ATL L7-4 probe (Philips, Bothell, WA) driven at 5 MHz.
- Using 21 angles (-5º to 5º) compounding,
- 100 frames were acquired for each phantom.
- Beamformed radiofrequency data were averaged over all frames.
- In this work, power spectra were averaged over 25 scanlines, each spanning 10 pulse lengths. Each ROI (height of 1 cm) was partitioned into 5 overlapping windows [1].

Comparison:

- The same acquisition were done on reference phantom in order to perform the spectral log deference method (SLD) according to [3].
- Ground truth ACS values were obtained from planar reflector method [2] (in dB/cm/MHz): #1) 0.56 $\pm$ 0.06 (4.5% graphite powder); #2) 1.27 $\pm$ 0.09 (12% graphite powder).



Construction of attenuation map by moving the red shaded computing window

[1] Gong P et al (2019) *IEEE TUFFC* 6: 867-875.
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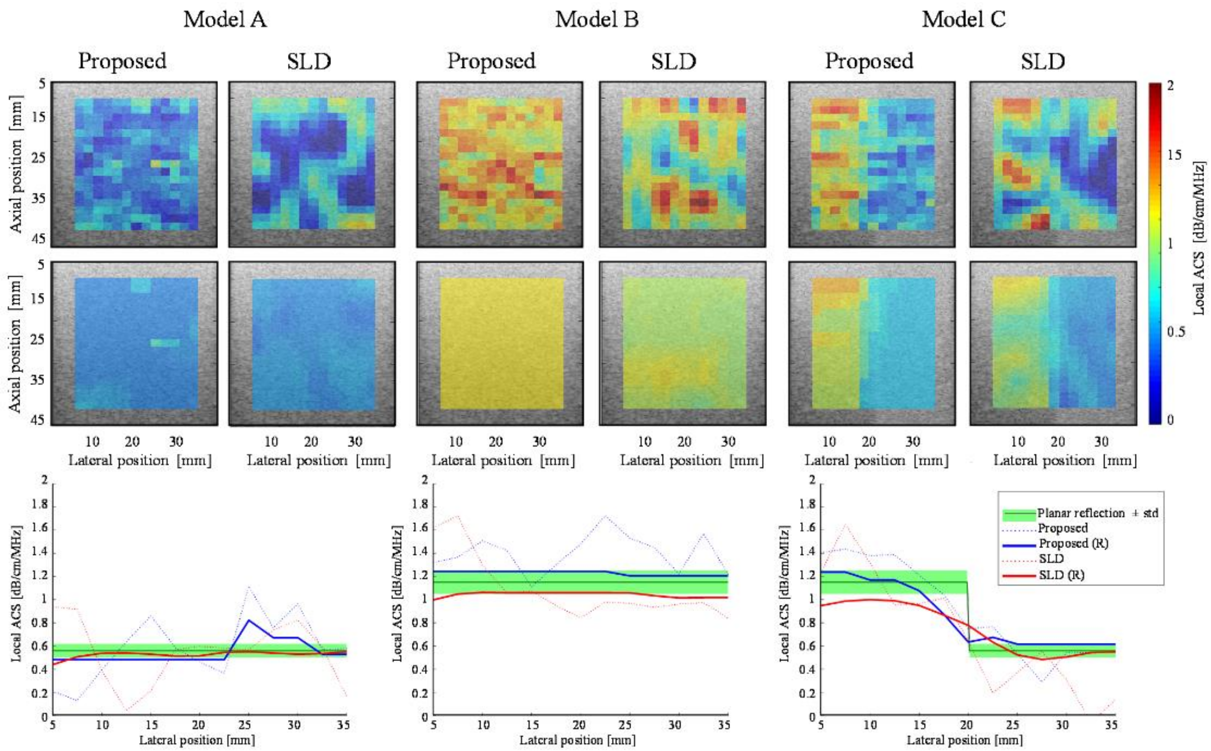
3. Results

Homogeneous & Side-by-side phantoms

Local attenuation maps obtained with PF and SLD methods for experimental phantoms with medium #1 (model A), medium #2 (model B), and side by side media #1 and #2 (model C). The first and second rows show attenuation maps without and with regularization, respectively. The bottom row presents the comparison of regularized (R) and non-regularized mean ACS estimated with both PF and SLD methods for the three models. Green regions in graphs of bottom row show means and standard deviations for ground truth measurements with the planar reflection method.



3. Results

Inclusion phantoms

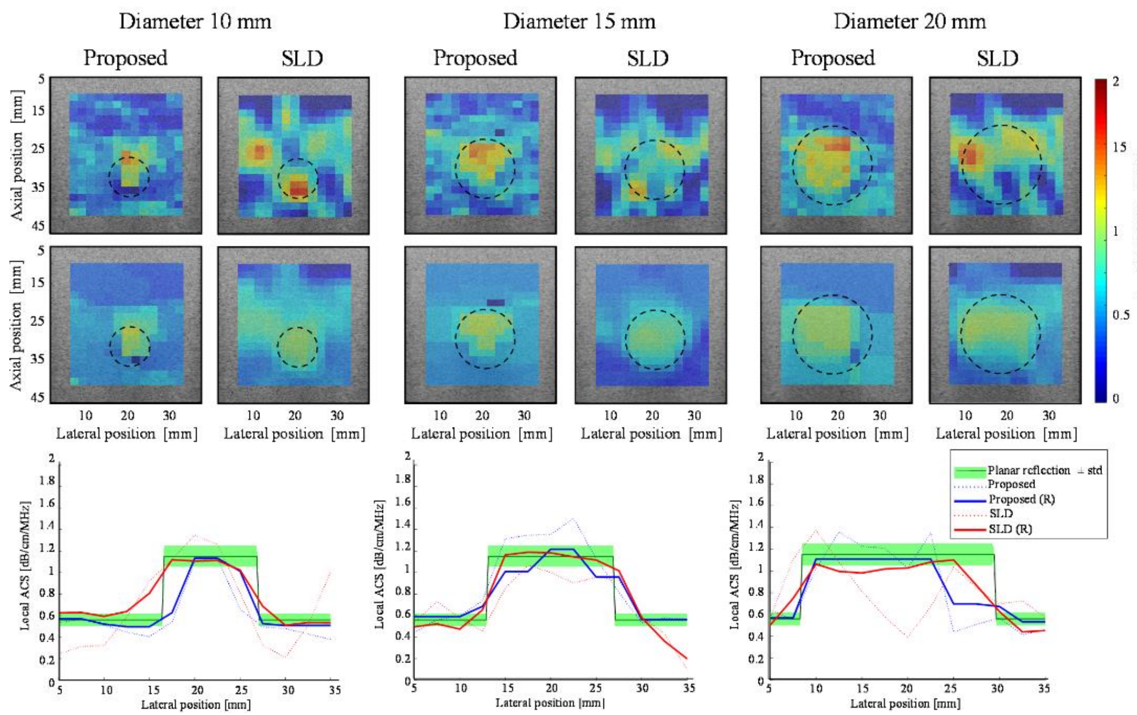
Local attenuation maps for experimental phantoms with inclusion diameters of 10 mm, 15 mm, and 20 mm with PF and SLD methods. The first and second rows show attenuation maps without and with regularization, respectively. The bottom row presents the comparison of regularized (R) and non-regularized mean ACS estimated with both PF and SLD methods for the three inclusion sizes. Green regions in graphs of bottom row show means and standard deviations for ground truth measurements with the planar reflection method.

- **One-way analysis of variance (ANOVA) with repeated measures**

Overall, mean of NRMSE values of PF and SLD methods from 55 experimental phantom data including homogeneous, side-by-side and inclusion phantoms were:

Methods	NRMSE (p <0.001)	Bias (p <0.001)
PF	40.86±10.63	0.20±0.12
PF-R	31.82±14.31	0.16±0.13
SLD	75.70±27.60	0.19±0.11
SLD-R	42.11±23.05	0.18±0.13

PF method with regularization has the lowest bias and NRMSE values and its attenuation estimation is more accurate compared to the other methods.



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4. Conclusion

- Tests conducted showed that the PF with regularization yielded robust results, suggesting its use as a diagnosis method.
- The main advantage of PF is the absence of calibration with a reference phantom, which is a significant add-on to improve the clinical workflow.
- It was shown that applying regularization overall improved local ACS maps.
- Future works will aim at addressing the in-vivo human liver datasets.

Thank you for your attention

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