## Research Plan

### A brief description of the subject and the scientific and technological background

Ultrasound signals that propagate through the anatomy can be used to calculate acoustic parameters such as sound speed and attenuation. This was recognized in the pioneering work of Greenleaf and his collaborators on ultrasound tomography ([Greenleaf *et al.* 1977](#_ENREF_14), [Greenleaf and Bahn 1981](#_ENREF_13)). A circular setup of sensors was proposed by ([Norton and Linzer 1979](#_ENREF_19)), and a ring system was built by ([Duric *et al.* 2007](#_ENREF_10)) and further developed for breast imaging at the Karmanos Cancer Institute, ([Duric *et al.* 2012](#_ENREF_9)). Another experimental setup was built by ([Gemmeke and Ruiter 2007](#_ENREF_12)). Diffraction was also taken into account in ultrasound tomography investigations ([Devaney 1982](#_ENREF_5), [1983](#_ENREF_6), [Simonetti *et al.* 2008](#_ENREF_23), [Simonetti *et al.* 2009](#_ENREF_24)). The above studies pointed at the observation that acoustic measurements made with transmission ultrasound could be used to characterize tissue. Studies on ultrasound tomography have revealed that parameters of sound speed and attenuation could help differentiate benign masses from cancer ([Duric *et al.* 2009](#_ENREF_8)).

Forward and inverse models of ultrasound tomography are quite complex. To accelerate tomographic reconstruction, certain approximations are required. At the high-frequency limit, the problem can be treated with optical geometry methods, such as the Eikonal equation ([Hamilton 1834](#_ENREF_15)). A direct numerical solution of the Eikonal equation has become a popular method of computing travel-times on regular grids, commonly used in seismic imaging ([Vidale 1990](#_ENREF_28), [Sethian and Popovici 1999](#_ENREF_21)).

Ultrasound travel-times can be calculated in this approximation by using bent rays ([Shengying *et al.* 2010](#_ENREF_22), [Li *et al.* 2009](#_ENREF_18))(Goldstein *et al.* 2002). The Eikonal equation is a non-linear differential equation ([Pinchover and Rubinstein 2005](#_ENREF_20)). A complete solution of the tomography problem in the Eikonal approximation would require solving a non-linear inverse problem ([Tarantola and Valette 1982](#_ENREF_26), [van Dongen and Verweij 2012](#_ENREF_27)). While the non-linear Eikonal equation can be used for the forward problem, an often made approximation is used for the inverse problem by invoking the Linear Eikonal equation ([Aldridge 1994](#_ENREF_1), [Fomel 1997](#_ENREF_11)). This approach takes full account of bent rays in the forward problem, while it takes the bending into account only approximately when treating the inverse problem. The investigators of this project propose using the linear approximation for the inverse problem as the starting point for the non-linear inversion algorithm. Preliminary calculations have shown that this approach is effective in getting convergence of the non-linear inversion process.

Tomographic images of sound speed are often obtained by neglecting effects of attenuation. However, the higher the ultrasound frequency the higher is the loss of amplitude, and the contribution of attenuation becomes significant. Experimental evidence indicates a power law behavior with an exponent in the interval 1 to 1.5 for sound wave attenuation in human tissue, ([Duck 1990](#_ENREF_7)). In order to explain such behavior, fractional wave equations with attenuation have been proposed by ([Caputo 1967](#_ENREF_2)), ([Szabo 1995](#_ENREF_25)), ([Chen and Holm 2003](#_ENREF_3), [Chen and Holm 2004](#_ENREF_4)), and ([Kelly and McGough 2008](#_ENREF_16), [Kelly *et al.* 2008](#_ENREF_17)). These equations capture the power law attenuation with frequency as observed in many experimental settings when sound waves travel through inhomogeneous media.

### Objectives and significance of the research

As mentioned in the background description, attenuation of ultrasound is very important, as it is a major factor in limiting the accessible depth for imaging. Attenuation is increased (and hence penetration of the beam reduced) for higher frequency (shorter wavelength) transducers. Standard (B-mode) ultrasound equipment intrinsically compensate for an expected average degree of attenuation by automatically increasing the gain (overall brightness or intensity of signals) for deeper areas in the anatomy.

Only a constant [average] value of the attenuation can be determined experimentally in B-mode ultrasound imaging. Measurements of the reflected signal alone (B-mode) do not contain enough information for determining the spatial dependency of attenuation in the anatomy. Tomography, namely taking into account scattering and transmission directions of the ultrasound waves, enables the measurement of attenuation. The objective of the research in this proposal is to develop new methods for calculating and measuring acoustic attenuation using ultrasound tomography and fractional wave equations.

### Comprehensive description of the methodology and plan of operation, including the respective roles of the Israeli and American principal investigators

The methodology of the research is based on time-fractional wave equations relating to power law media with an attenuation coefficient that depends on the location in the medium (a function of , ) given by

|  |  |  |
| --- | --- | --- |
|  |  | (1) |

One example we intend to use is the following time-fractional wave equation ([Kelly *et al.* 2008](#_ENREF_17)), which exactly satisfies equation (1) for all frequencies . For and with a location-dependent velocity of sound , the power law wave equation for inhomogeneous media is written as

|  |  |  |
| --- | --- | --- |
|  | . | (2) |

This equation has a spatially dependent wavenumber given by

|  |  |  |
| --- | --- | --- |
|  | . | (3) |

The imaginary part of equation (3) yields the power law attenuation described by equation (1) and the real part yields the frequency-dependent wave velocity ([Kelly *et al.* 2008](#_ENREF_17)), ,

|  |  |  |
| --- | --- | --- |
|  | . | (4) |

Taking the temporal Fourier Transform of equation (2) with representing the Fourier Transform of in time,

,

we have

|  |  |  |
| --- | --- | --- |
|  | . | (5) |

Defining to be a generalized complex *refractive index* that depends on space and frequency by the following expression

|  |  |  |
| --- | --- | --- |
|  | . | (6) |

We note that

|  |  |  |
| --- | --- | --- |
|  | . | (7) |

we arrive at the homogeneous Helmholtz equation

|  |  |  |
| --- | --- | --- |
|  | . | (8) |

As in the case of the standard Helmholtz equation, the frequency picture contains powers of the frequency instead of the time-domain derivatives. This results in wave propagation equations that do not require algorithms that explicitly handle the fractional derivatives.

By considering a solution of the form

|  |  |  |
| --- | --- | --- |
|  | , | (9) |

where is the amplitude and is the travel-time one obtains the following two coupled equations

|  |  |  |
| --- | --- | --- |
|  | . | (10) |
|  | , | (11) |

In the high-frequency limit, the middle term of equation (10) can be neglected, and we obtain a frequency-dependent Eikonal Equation that is independent of the amplitude ,

|  |  |  |
| --- | --- | --- |
|  | . | (12) |

Equations (11) and (12) are [one-way] coupled, i.e. the gradient solved for in the Eikonal equation (12) should be inserted in the transport equation (11).

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