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Suggestion of Ultrasonic System for Diagnosis of Functional Gastrointestinal Disorders: Finite Difference Analysis, Development and Clinical Trials

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***Abstract*—**The disaster from functional gastrointestinal disorders has detrimental impact on the quality of life of the effected population and imposes a tremendous social and economic burden. There are, however, rare diagnostic methods for the functional gastrointestinal disorders. Our research group identified recently that the gastrointestinal tract well in the patients with the functional gastrointestinal disorders becomes more rigid than healthy people when palpating the abdominal regions overlaying the gastrointestinal tract. Objective of current study is, therefore, identify feasibility of a diagnostic system for the functional gastrointestinal disorders based on ultrasound technique, which can quantify the characteristics above.

Two-dimensional finite difference (FD) models (one normal and two rigid model) were developed to analyze the reflective characteristic (displacement) on each soft-tissue layer responded after application of ultrasound signals. The FD analysis was then based on elastic ultrasound theory. Validation of the model was performed via comparison of the characteristic of the ultrasonic responses predicted by FD analysis with that determined from the actual specimens for the normal and rigid conditions. Based on the results from FD analysis, ultrasound system for diagnosis of the functional gastrointestinal disorders was developed and clinically tested via application of it to 40 human subjects with/without functional gastrointestinal disorders who were assigned to Normal and Patient Groups.

The FD models were favorably validated. The results from FD analysis showed that the maximum displacement amplitude in the rigid models (0.12 and 0.16) at the interface between the fat and muscle layers was explicitly less than that in the normal model (0.29). The results from actual specimens showed that the maximum amplitude of the ultrasonic reflective signal in the rigid models (0.2±0.1Vp-p) at the interface between the fat and muscle layers was explicitly higher than that in the normal model (0.1±0.0Vp-p). Clinical tests using our customized ultrasound system showed that the maximum amplitudes of the ultrasonic reflective signals near to the gastrointestinal tract well for the patient group (2.6±0.3Vp-p) were generally higher than those in normal group (0.1±0.2Vp-p). Here, maximum reflective signals was appeared at 20mm depth approximately from abdominal skin for all human subjects, corresponding to the location of the boundary layer close to gastrointestinal tract well. These findings suggest that our customized ultrasound system using the ultrasonic reflective signal may be helpful to the diagnosis of the functional gastrointestinal disorders.

***Keywords*—**Finite Difference (FD) Analysis, Functional Gastrointestinal Disorders, Gastrointestinal Tract, Ultrasonic Responses.

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I. Introduction

FUNCTIONAL gastrointestinal disorders affect millions of people spread all age regardless of race and sex [1]. The functional disorders refer primarily to an alerted physiological function rather than an identifiable structural or biochemical causes [1]. The functional gastrointestinal disorders are, therefore, characterized by chronic symptoms referable to gastrointestinal tract in absence of currently recognized biochemical or structural explanations [2, 3]. This fact makes it difficult to diagnose the functional gastrointestinal disorders by the traditional examinations such as x-ray or laboratory tests (i.e., blood test). It may lead to misdiagnosis and misguided treatment. The method for the accurate diagnosis of the functional gastrointestinal disorders is, therefore, necessarily

developed.

Ultrasound, a form of mechanical energy that is transmitted through and into biological tissues as an acoustic pressure wave, is used widely in medicine as a therapeutic, operative, and diagnostic tool [4]. Therapeutic ultrasound uses intensities as high as 1 to 3W/cm^2 and can cause considerable heating in living tissues to reduce pain and muscle spasms, and to improve muscle mobility. The ultrasound as a surgical instrument uses higher levels of intensity of 5 to 300W/cm^2 to fragment calculi, to initiate the healing of non-unions, to ablate diseased tissues such as cataracts. Diagnostic ultrasound use much lower magnitudes of 1 to 50mW/cm^2 to image non-invasively vital organs, fetal development, peripheral blood flow, and metabolic bone diseases and, coincidentally, to evaluate fracture callus during healing. The intensity level used for imaging is regarded as non-thermal and non-destructive [5]. At the present time, various therapeutic, operative, and diagnostic methods using ultrasound characteristics have been still developing, and their effectiveness have been identifying in practical clinics. These facts indicate that ultrasound technique may be challengeable in the development of the accurate diagnostic system for the functional gastrointestinal disorders.

Our research group identified recently that the gastrointestinal tract well in patients with the functional gastrointestinal disorders becomes more rigid than that in healthy people when palpating the abdominal regions overlaying the gastrointestinal tract well. Objective of current study is, therefore, identify feasibility of a diagnostic system for the functional gastrointestinal disorders based on ultrasound technique, which can quantify the characteristic above related to the rigidity of the gastrointestinal tract well.

II. Materials and Methods

A. Development of Finite Difference (FD) Models

A FD model (normal model) for the normal condition was created based on geometric and material information measured from the actual specimens (Fig. 1). The model consisted of three soft-tissue layers making up the overall object, skin, fat and muscle, going from top to bottom across the model. Material properties required for the analysis were summarized in Table I. Density (ρ) and longitudinal bulk acoustic wave velocity (VL) for each soft-tissue were determined from literatures [6]. Based on the determined ρ and VL, first and second lame constants (λ *and* μ), related to elastic constants (*i.e., Young's modulus and Poisson' ratio*) used commonly in Finite Element analysis, were computed using following equations (1) and (2).

$$\lambda = \rho \times (VL^2 - 2 \times VT^2) \quad (1)$$

$$\mu = \rho \times VT^2 \quad (2)$$

Here, μ was considered as zero value corresponding to *Poisson' ratio* of 0.5, which represents incompressibility of soft-tissue materials [7-9]. One infinite (absorbing) boundary condition was employed at bottom of the FD model (Fig. 1). For loading condition, sine pulse (source signal) of 5MHz frequency (*Maximum Amplitude = 1*) produced from the transducer defined over the skin layer was applied one time to the FD model during 0.1μs (Figs. 1 and 2). The sign pulse is a specification of a time-dependant displacement, corresponding to a mechanical response induced by the ultrasound signal generated from the actual transducer of the ultrasound system [7, 8]. Three receivers were defined at the top of the FD model and the interfaces between the soft-tissue layers to predict displacements, which corresponding to the source signal, at locations of interest in the object (Fig. 1). Here, the displacement amplitude predicted at the receiver is inversely proportional to the amplitude of the ultrasonic reflective signal obtained by the receiver in the actual ultrasound system [7, 8].

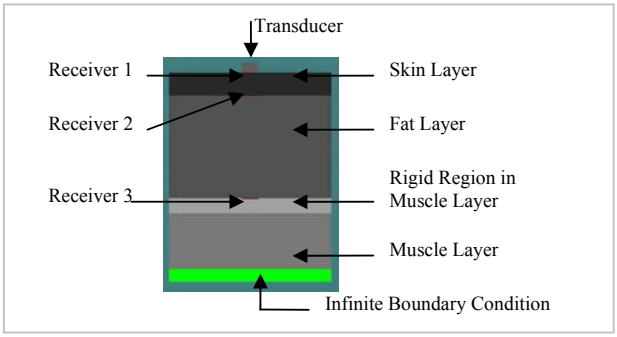

Fig. 1 Two-Dimensional FD model and its elements; Model type (normal or rigid model) was determined with the material properties used in the rigid region in the muscle layer

TABLE I
Material Properties for the Finite Different Models [6]

Layers		ρ (g/cm^3)	VT (m/s)	λ (N/mm^2)	μ (N/mm^2)
Skin		1000	1519	2307	0
Fat		920	1478	2010	0
Muscle	Normal Model	1040	1552	2505	0
	Rigid Model 1	1040	2328	5636	0
	Rigid Model 2	1040	3104	10020	0

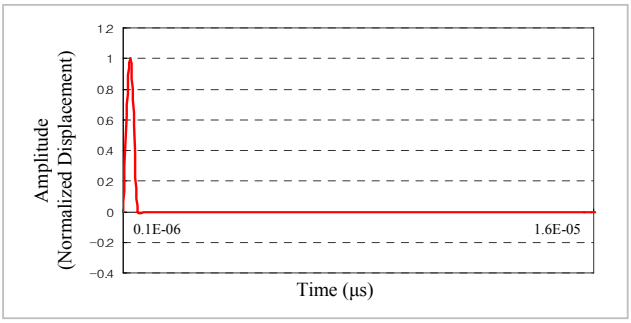

Fig. 2 Source signal (5MHz frequency with amplitude of 1) applied to the FD models during 0.1μs

Additionally, two FD models (rigid models) were created representing a rigidity of the gastrointestinal tract well induced by the functional gastrointestinal disorders (Fig. 1). It was to predict alterations in the characteristics of the ultrasonic reflective signals in the rigid conditions. Unfortunately, because there was no information related to the material properties for the rigid conditions, assumed material properties were used in current study (Table I). The assumption related to the material properties for the rigid models, was based on the fact that the gastrointestinal tract well may be contracted continuously by breakdown in the Ca^{2+} pump regulation [10-13]. This may increase elastic characteristics of smooth muscle as a structural element of the gastrointestinal tract well. Based on this assumption, two first lame constants were selected for the rigid models as shown in Table I. Here, it was assumed that densities were not altered for the rigid models, because the intrinsic material characteristics may be not changed. Other parameters (*i.e., Boundary and Loading Conditions*) used for the rigid models were same as those in the normal model.

All FD analyses were conducted using stand-alone computer software package (Wave2000 Pro™, CyberLogic Inc., USA) that generates solutions to practically any 2D ultrasonic (elastic wave propagation) problem.

B. Validation of Finite Difference (FD) Model

Validation of FD model was performed via comparison of an alteration in the characteristics of the ultrasonic responses predicted by FD analyses with that determined from the actual ultrasound system, induced by a change of the rigidity in the FD models and the specimens. The ultrasound system was designed based on the results from the FD analysis.

Ten soft-tissue specimens were harvested from porcine. Five of them were then treated chemically to mimic a rigid condition of gastrointestinal tract well, which was induced by the functional gastrointestinal disorders. A chemical liquid was injected to the interface between the fat and muscle layers to mimic the rigid condition. This chemical treatment made it possible to harden a region of the muscle layer in the specimens. The specimens consisted of three soft-tissue layers making up the overall object, skin, fat and muscle, going from top to bottom (Fig. 3). Dimension of the specimens was 20 x 20 x 21 mm approximately.

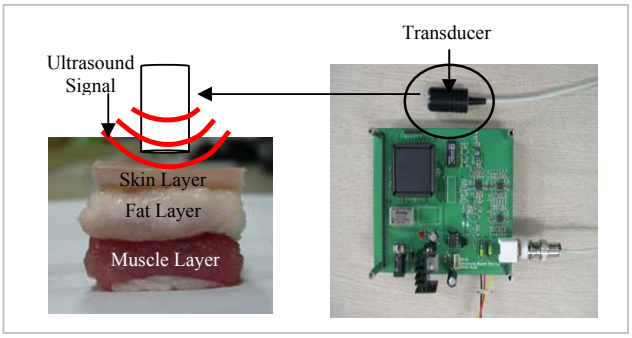

Fig. 3 Configuration of the test using actual ultrasound system (right) for the actual specimen (left); For the rigid condition of the specimen, a chemical liquid was injected to the interface between the fat and muscle layers

Ultrasound signal was applied to the specimens using the actual ultrasound system (*ultrasonic test*) (Fig. 3). The ultrasound system consisted of following main elements: transducer, transmitter, low-noise amplifier (LNA), band-pass filter (BPF), time gain compensator (TGC) and complex programmable logic device (CPLD) for control of the system. For the validation, the ultrasound signal corresponded to the source signal used in the FD analysis was applied to the specimen.

Additionally, *in-vitro compressive test* using Instron Microtest System (5848 series, Instron, Norwood, MA, USA) was performed for all specimens (Fig. 4). It was performed to identify whether or not the specimens were well treated chemically for representation of the rigid condition of them. The compressive loads corresponded to $0.01s^{-1}$ strain rate were applied continuously to the specimens. Pre-cycling was then applied three times just before the compression test, to adjust specimen location and reduce viscoelastic characteristics. Non-linear hyperelastic material model (*First Order Ogden Model*) was used to describe mechanical characteristics for the normal and rigid conditions. The hyperelastic material model was based on the following strain energy function U:

$$U = \frac{2\mu_1}{\alpha_1^2}(\bar{\lambda}_1^{\alpha_1} + \bar{\lambda}_2^{\alpha_1} + \bar{\lambda}_3^{\alpha_1} - 3) + \frac{1}{D}(J^{el} - 1)^2 \qquad (3)$$

U: strain energy per unit of reference volume,
μ_1 *and* α_1: temperature-dependent material parameters,
J^{el}: elastic volume ratio,
$\bar{\lambda}_i = J^{-1/3}\lambda_i$: deviatoric stretches, and
λ_i: principal stretches.

For statistical analysis, a paired student's t-test was used to identify a significant difference between the results obtained from the normal and rigid conditions of the actual specimens, for *both ultrasonic* and *compressive tests*. The significance levels were then set at 0.05 for all tests.

Fig. 4 Configuration of the compressive test using Instron Microtest System (5848 series, Instron, Norwood, MA, USA)

C. Clinical Trials using Customized Ultrasound System

The customized ultrasound system was tested clinically via application to human subjects with/without the functional gastrointestinal disorders. It was performed to finally identify feasibility of utilization of the customized ultrasound system for diagnosis of the functional gastrointestinal disorders in practical clinics.

Following Institutional Review Board approval, 40 female human subjects (43.3±12.4 years) were randomized into two groups: 20 normal subjects were assigned to control group and 20 patient subjects with symptoms related to the functional gastrointestinal disorders were assigned to patient group.

Same region on the abdomen of the human subjects was selected and palpated using the customized ultrasound system (Fig. 5). The ultrasonic reflective signals were then acquired by a monitoring program customized by Labview 7.1 (National Instruments, Austin, Texas, USA). It was analyzed via comparison of the reflective signals obtained from the normal and patient groups. Here, a paired student's t-test was used to identify a significant difference between the normal and patient groups. The significance level was then set at 0.05.

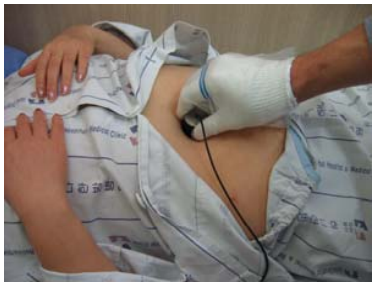

Fig. 5 Palpation on the abdomen using the customized ultrasound system for diagnosis of the functional gastrointestinal disorders

III. Result

A. Results of Finite Difference Analysis and Validation

Fig. 6 showed the ultrasonic responses for one normal and two rigid models predicted by FD analyses. The maximum displacement amplitudes at the interface between the fat and muscle layers (*Receiver 3*) were decreased 55.5% (normal model), 69.5% (rigid model 1), and 75.1% (rigid model 2) relative to that at the interface between the skin and fat layers (*Receiver 2*). The alterations of the maximum displacement amplitudes, which were induced by a change of the rigidity, were 14.0% between the normal model and rigid model 1 and 19.6% between the normal model and rigid model 2.

Fig. 7 showed the representative ultrasonic responses for the normal and rigid specimens determined from the actual ultrasound system. The maximum amplitudes of the ultrasonic reflective signals at the interface between the fat and muscle layers were decreased 62.4±10.9% (normal specimens) and 36.9±27.7% (rigid specimens) relative to that at the interface between the skin and fat layers. There was a significant difference between the results obtained from the normal and rigid specimens ($p<0.05$). Unlike the results from the FD analyses, the maximum amplitude of the ultrasonic reflective signal at the interface between the fat and muscle layers relative to that at the interface between the skin and fat layers was decreased with increase of rigidity of the specimens. It is because the displacement amplitude predicted from the FD analysis is inversely proportional to the amplitude of the ultrasonic reflective signal obtained. The alteration of the maximum amplitudes of the ultrasonic reflective signals, which were induced by a change of the rigidity, was average 25.5% between the normal and rigid specimens. These findings from the ultrasonic tests were favorably corresponded to the results obtained from the FD analyses.

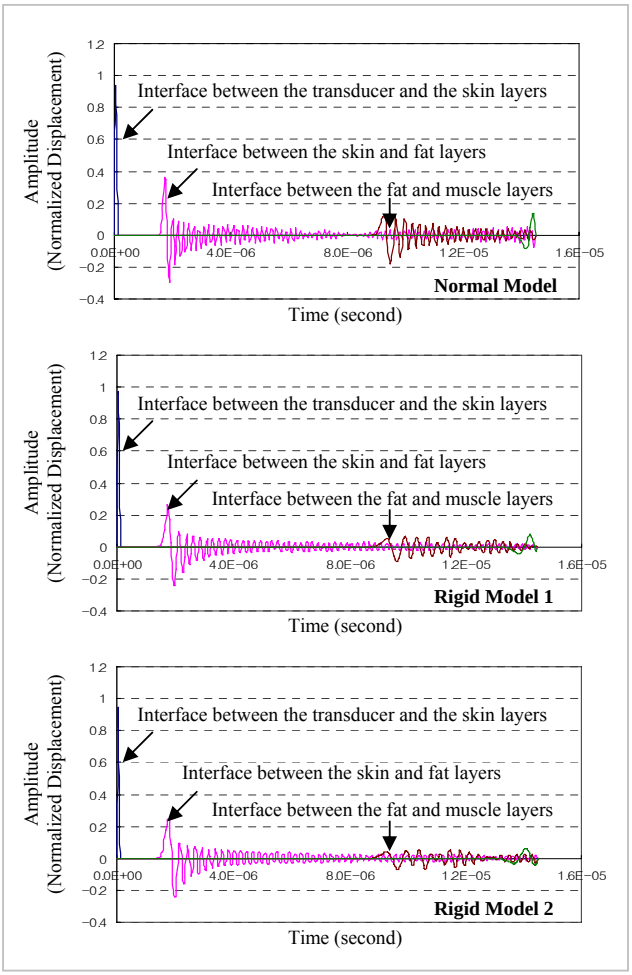

Fig. 6 Ultrasonic responses for the normal and two rigid models predicted by FD analyses

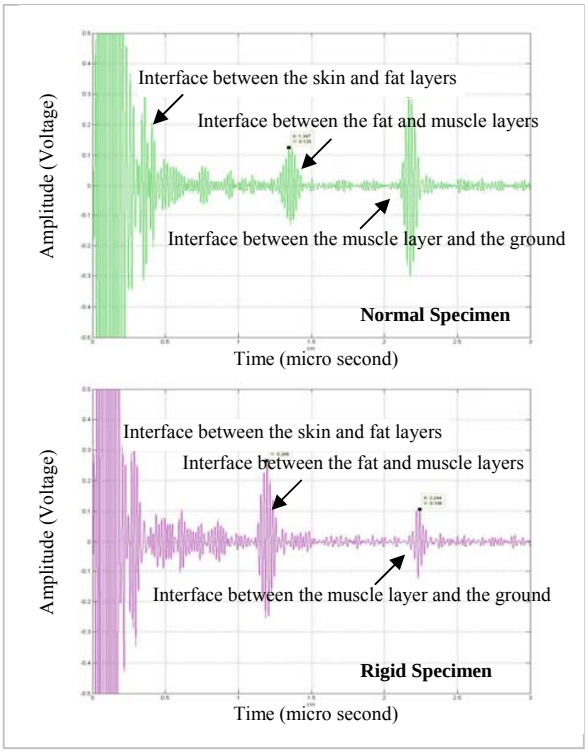

Fig. 7 Representative ultrasonic responses for the normal and rigid specimens determined from the actual ultrasound system

Fig. 8 showed stress-strain curves drawn from the hyperelastic material model (*First Order Ogden Model*) determined from the compressive tests. It was identified that the rigid specimens (μ_1: 1.1±0.2MPa and α_1: 18.5±2.4) were generally more rigid than the normal specimens (μ_1: 0.5±0.3MPa and α_1: 19.5±1.9) ($p<0.05$). Here, there was no significant difference between α_1 values determined for the normal and abnormal groups ($p>0.05$). This finding indicates that the specimens treated to represent the rigid conditions were reliable.

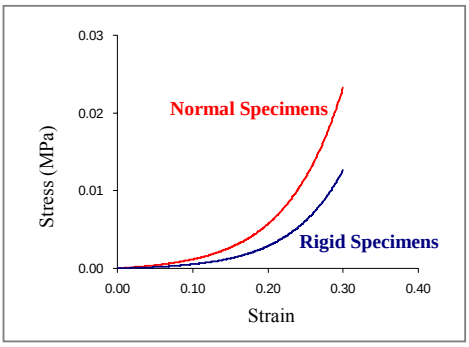

Fig. 8 Stress-Strain curves drawn from the hyperelastic material model determined from the compressive tests; the hyperelastic material model was used for presentation of non-linear mechanical characteristic of the specimens

B. Clinical Results

Fig. 9 showed the representative ultrasonic responses for the normal and patient groups. For the normal group, the maximum amplitudes of the ultrasonic reflective signals at the boundary of the gastrointestinal tract well (0.1±0.2Vp-p) were similar to those at the skin and fat layers (0.2±0.3Vp-p) ($p>0.05$). This indicates that the material characteristics (*i.e., density, acoustic impedance, and elastic modulus*) are similar for all soft-tissues inside the abdomen. For the patient group, the maximum amplitudes of the ultrasonic reflective signals at the boundary of the gastrointestinal tract well (2.6±0.3Vp-p) were high relative to those at the skin and fat layers (0.3±0.2Vp-p) ($p<0.05$). This finding may indicate that the gastrointestinal tract well is rigid due to reasons induced by the functional gastrointestinal disorders. The reasons will be discussed at following section. The results showed that the maximum reflective signals at the boundary near to the gastrointestinal tract well for the patient group were generally higher than those in the normal group ($p<0.05$). Here, the maximum amplitudes of the ultrasonic reflective signals at the boundary of the gastrointestinal tract well were generally appeared at 20mm depth approximately from abdominal skin for all human subjects. This finding was favorably corresponded to the location of the boundary of the actual gastrointestinal tract well.

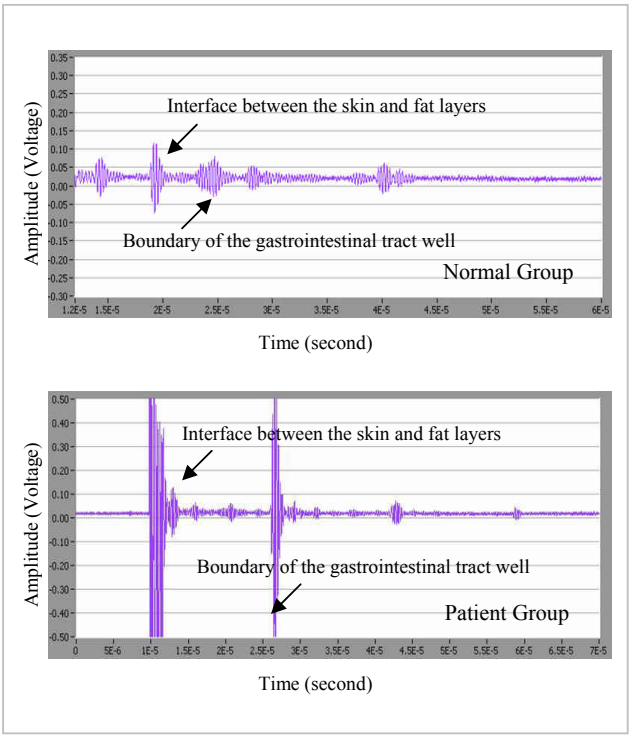

Fig. 9 A representative reflective signal of ultrasound for normal and patient groups

IV. Discussions and Conclusion

Current study shows the customized ultrasound system may be able to detect effectively an alteration of rigidity in the gastrointestinal tract well, which can be induced by the functional gastrointestinal disorders. It can be supported the explicit fact that characteristics of ultrasound responses are changed corresponding to alterations in materials composed objects. However, it has been not attempted to identify a degree of progress of the functional gastrointestinal disorders using the characteristics of the ultrasound responses described above. It may be due to difficulty in identification of symptoms (*i.e., rigidity of the gastrointestinal tract well identified in this study*) of the functional gastrointestinal disorders. This study may be, therefore, valuable as first attempt to diagnose quantitatively the functional gastrointestinal disorders.

The number of patients who have the functional gastrointestinal disorders is increasing in recent years. The functional gastrointestinal disorders induce directly abnormal function in gastrointestinal motility, which is defined by the movement of the digestive system, and the transit of the contents within it [1]. This abnormal gastrointestinal motility can develop various symptoms (*i.e., heartburn, nausea, constipation, dyspepsia, tympanites, vomiting, and diarrhea*), resulting in leaving the patients unable to fully participate in life and work in a severe case. This abnormal gastrointestinal motility may also produce a toxin, which can be absorbed into the gastrointestinal tract, resulting in a breakdown in the function of the nerve and cellular system in any portion of gastrointestinal tract. The consecutive breakdown may cause physiological problems in the gastrointestinal tract well (*i.e., rigor of the tract well*).

Our research group identified recently that the gastrointestinal tract well in patients with the functional gastrointestinal disorders becomes more rigid than that in healthy people when palpating the abdominal regions overlaying the gastrointestinal tract well. This may be explained by the pacemaker mechanisms underlying the gastrointestinal autonomic rhythmic motility. It is widely accepted that Interstitial Cells of Cajal (ICC) drives spontaneous rhythmic motility in the integrative control of the gastrointestinal function [11, 13]. Here, this ICC form networks widely distributed within the submucosal, intra-muscular and inter-muscular layers of the gastrointestinal tract well from the esophagus to the internal anal sphincter [11, 13]. Considerable researchers reported the ICC affected intracellular Ca^{2+} handling, which plays a critical role in generation of pacemaker for the spontaneous rhythmic motility, although respective players such as the Ca^{2+}-ATPase of the sarcoplasmic reticulum (endoplasmic reticulum), IP3 receptors, ryanodine receptors and plasma membrane ion channels might have divergent roles in the Ca^{2+} release-refilling cycles [10, 12, 13]. Based on these facts, it may be expected that abnormalities of the ICC induced by a toxin absorbed into the gastrointestinal tract well generate abnormal function of intracellular Ca^{2+} handling. This may result in a rigor of the gastrointestinal tract well by abnormally

successive contraction of the smooth muscle composed the tract well. It is because the contraction of the smooth muscle is controlled by the excitation-contraction coupling mechanism regulated by Ca^{2+} pump [14].

There are limitations related to following issues; 1) in material properties in the FD models used for representation of the rigid conditions, 2) in chemical treatment to simulate the rigid condition in the actual specimens 3) in assumption of the reasons related to the change of the rigidity of the gastrointestinal tract well. These limitations will be solved through our ongoing study incorporated with molecular biological studies related to the functional gastrointestinal disorders.

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REFERENCES

[1] International Foundation for Functional Gastointestinal Disorders. "Gastointestinal functional and motility disorders". *Available:* http://www.iffgd.org/GIDisoders/Glmain.html 2006.
[2] N. J. Talley, V. Stanghellini, R. C. Heading, K. L. Koch, J. R. Malagelada, and G. N. Tytgat. "Functional gastrointestinal disorders". *Gut,* 45:1137-1142, 1999.
[3] W. G. Thompson, G. F. Longstreth, D. A. Drossman, K. W. Heaton, E. J. Irvine, and S. A. Muller-Lissner. "Functional bowel disorders and functional abdominal pain". *Gut,* 45:1143-1147, 1999.
[4] C. Rubin, M. Bolander, J. Ryaby, and M. Hadjiargyrou. "The use of low-intensity ultrasound to accelerate the healing of fractures". *J. Bone Joint Surg.,* 83A:259-270, 2001.
[5] R. St John Brown. "How safe is diagnostic ultrasonography". *J Can Med Assoc,* 131:307-311, 1984.
[6] J. F. Lehmann. "*Therapeutic Heat and Cold: Rehabilitation Medicine Library*". 4th ed. Williams & Wilkins, Baltimore, 1990.
[7] B. A. Auld. "*Acoustic fields and waves in solids*". 2nd ed, vol. 1-2. Krieger Publishing Company, Malabar, 1990.
[8] R. S. Schechter, H. H. Chaskelis, R. B. Mignogna, and P. P. Delsanto. "Real-time parallel computation and visualization of ultrasonic pulses in solids". *Science,* 265:1188-1192, 1994.
[9] C. W. Oomens, O. F. Bressers, E. M. Bosboom, C. V. Bouten, D. L. Blader, and E. T. N. c. w. j. o. t. n. Eindhoven University of Technology. "Can loaded interface characteristics influence strain distributions in muscle adjacent to bony prominences?" *Computer methods in biomechanics and biomedical engineering.,* 6(3):171-80, 2003.
[10] K. D. Keef, D. C. Murray, K. M. Sanders, and T. K. Smith. "Basal release of nitric oxide induces an oscillatory motor pattern in canine colon". *J. Physiol.,* 499:773-786, 1997.
[11] K. W. Min, and M. Leabu. "Interstitial Cells of Cajal (ICC) and Gastrointestinal Stromal Tumor (GIST): facts, speculations, and myths." *J. Cell Mol Med. ,* 10:995-1013, 2006.
[12] T. K. Smith, J. B. Reed, and K. M. Sanders. "Interaction of two electrical pacemakers in the muscularis of the canine proximal colon". *Am. J. Physiol.,* 252:C290-C299, 1987.
[13] M. Takaki. "Cut pacemaker cells: the interstitial cells of cajal (ICC)". *J. Smooth Muscle Res.,* 39:137-161, 2003.
[14] A. C. Guyton, and J. E. Hall. "*Textbook of medical physiology*". 10 ed. W.B. Saunders, Philadelphia, 2000.