



Research paper

Experimental study of the effect of the boundary conditions of fractured bone

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ABSTRACT

Reliable fracture diagnosis monitoring and analyzing low-frequency transverse vibration data can be achieved through an in-depth understanding of the physical interactions between wave propagation and boundary conditions. The present study aims to investigate the effects of the boundary conditions on the low-frequency structural vibrations of bones. Time–frequency domain analysis of transverse vibration signals depending on the boundary conditions of bones is analyzed and investigated. These studies reveal that the responses of fractured or non-fractured bones are different and influenced by the displacement and force boundary conditions. These relationships can be considered in the development of a smart fracture diagnosis system considering the posture and boundary condition. To validate the present observations, the experiments with artificial specimens and cadaver are carried.

1. Introduction

The present study presents the investigations of fracture diagnostics by low-frequency based health monitoring considering material properties, geometry, force and boundary condition. Some orthopedic doctors including the authors faced difficulties in reliably and frequently identifying the damage and modal parameters of peoples and assessing fracture healing rigorously as they are time-varying data due to the time varying material properties and posture. Various medical gold standard techniques such as X-ray, CT (Computed tomography), positron emission tomography (PET) and low-frequency vibration technique exist to diagnose various pathological and trauma-induced conditions (Toney et al., 2016; Ali, 2019; Dimililer, 2017) and references therein (Yoon et al., 2021). The present study employs the analysis of the low-frequency vibration data as an alternative to these gold standard medical techniques (Casaccia, 2015). An application of high-speed synchrotron X-ray phase contrast imaging in real-time damage characterization is studied with glass fiber reinforced composites subjected to dynamic loading (Gao et al., 2021). Femur bone is diagnosed with non-contact vibration-based approach using position detection approach (Gautam and Rao, 2021). Synthetic tibial cortical bone is investigated to diagnose bones for fractures, osteoporosis and healing with interaction between high-amplitude low frequency vibration and low-amplitude high frequency guided waves (Guha et al., 2020). Acoustic-based approach is employed to distinguish between

fractured and whole bones using digital signal processing and machine learning (Boger et al., 2020). To assess bone healing in fractures, the feasibility of the mechanical vibration method is proposed (Mattei et al., 2019). Time–frequency domain analysis of the vibration signals depending on the boundary conditions of bones is investigated. Comparing the vibrations with the ideal straight posture and boundary condition, it reveals that the responses of fractured or non-fractured bones are influenced. In real medical situation, however, patients experience the difficulties in making their bodies to the measurement positions for various different reasons such as pain, fracture position or different characteristics in medical devices. From a mechanical engineering point of view, the differences in the responses due to the different boundary condition are naturally accepted but from a medical engineering point of view, it also becomes an issue how to analyze the effect of the boundary condition or the posture to vibration data. The effects and relationships of the boundary conditions can potentially be explored for the development of a smart fracture diagnosis system considering the posture and boundary conditions of bones. Thus, this research conducts some experiments in order to observe the effects of the boundary conditions. To validate the present observations, some experiments with artificial specimens, animal legs, and a cadaver are carried out.

Some relevant researches about the application of low-frequency transverse vibrations to diagnose bone fracture and degenerative characteristics in non-medical environments can be found (Nokes, 1999).

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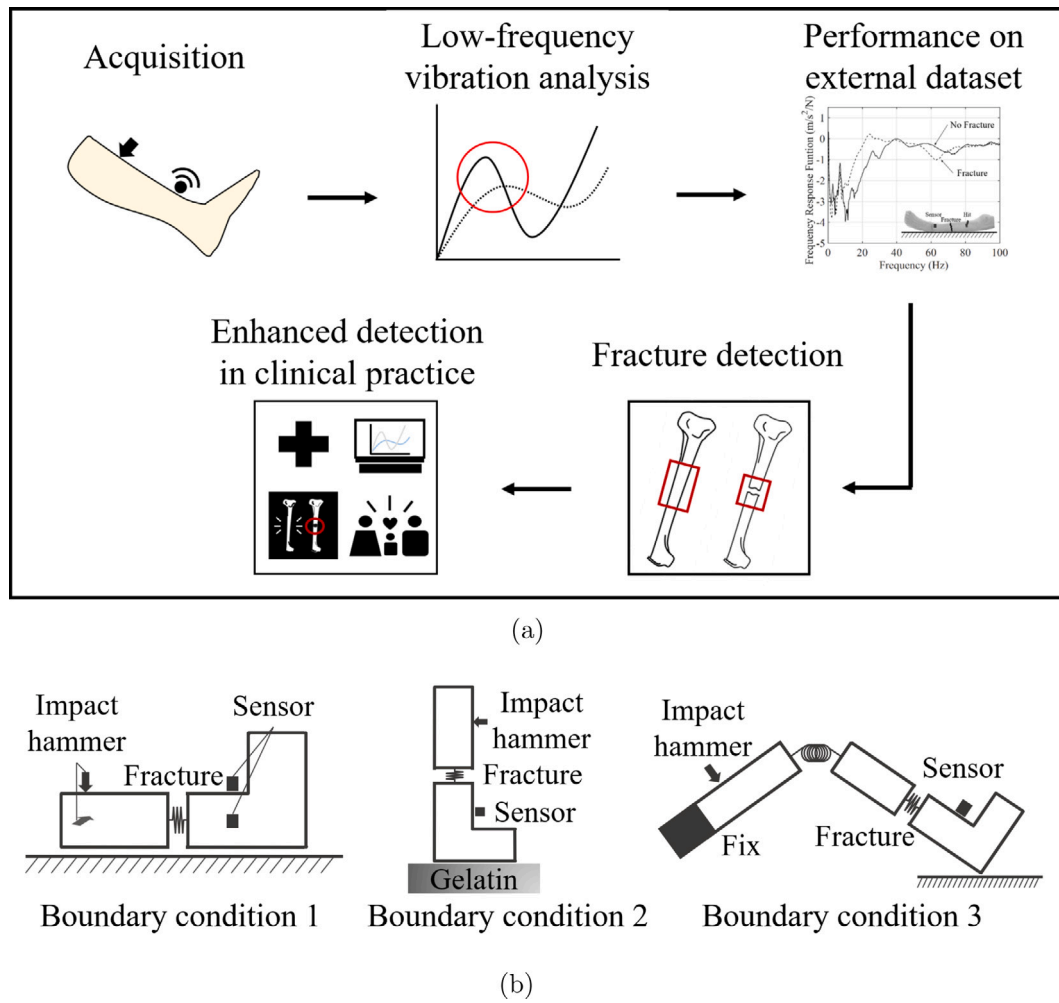


Fig. 1. (a) Diagnosis system with low-frequency vibration and (b) the three boundary conditions considered in the present study (Boundary condition 1: lying down in contact with ground, Boundary condition 2: standing condition on shoe and Boundary condition 3: bent leg condition).

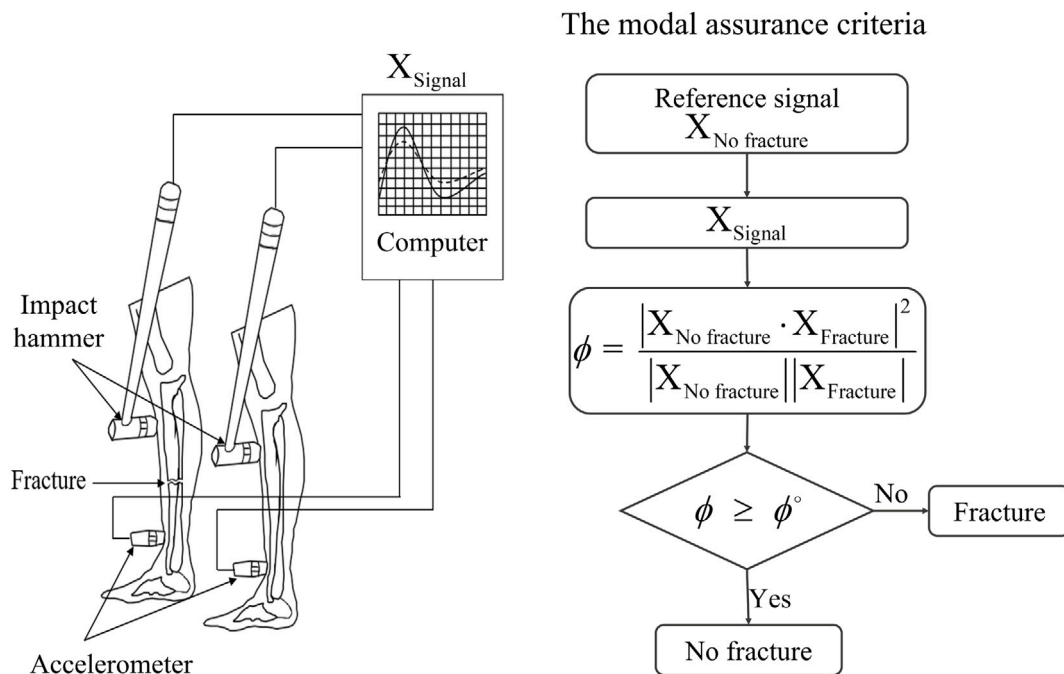


Fig. 2. Determination process based on the modal assurance criterion (MAC).

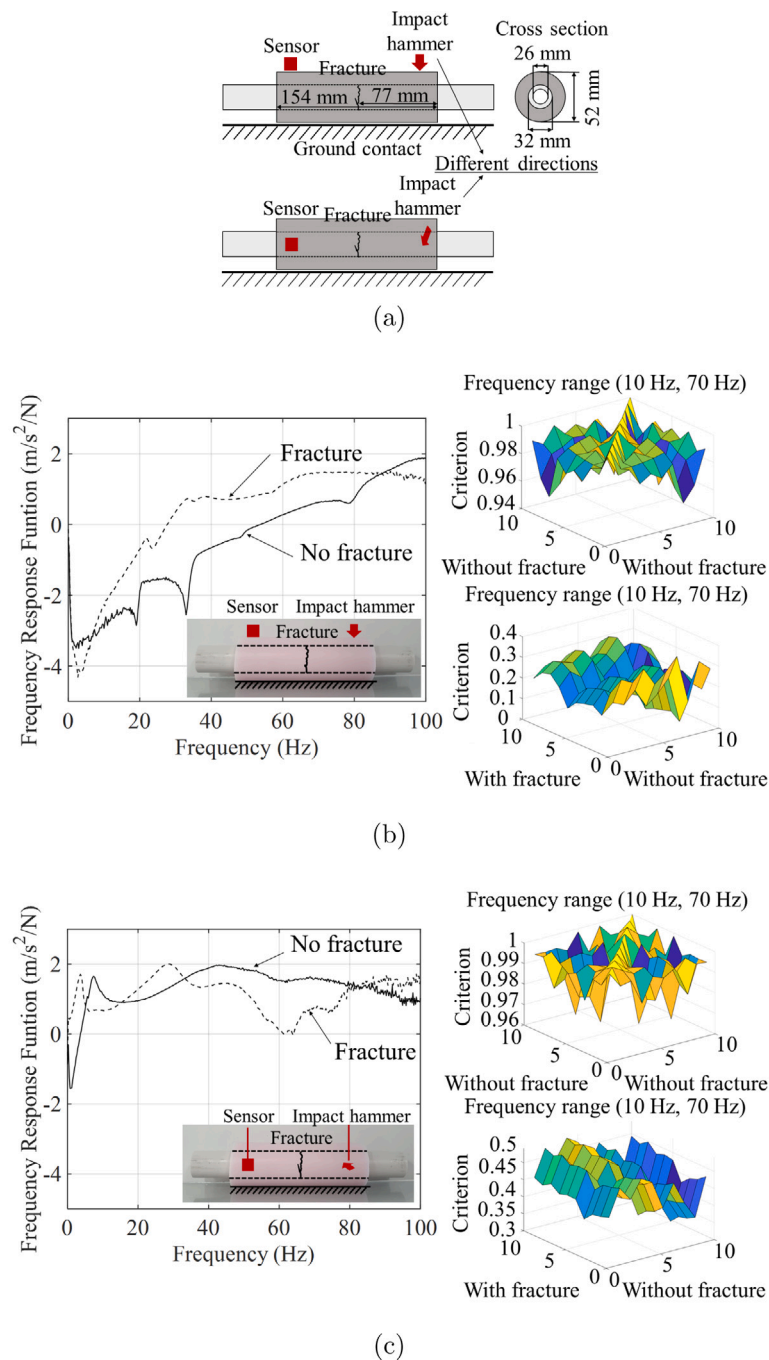


Fig. 3. Experiments with plastic bar and silicon. (a) Plastic bars and silicon specimens, (b) the responses with the sensor and the actuator attached to the vertical direction load and (c) the responses with the sensor and the actuator attached to the horizontal direction load.

Accurate and expensive medical techniques can accurately monitor various pathological and trauma-induced conditions with the side effect of the exposing the radiation. To diagnose the mechanical conditions of bone without exposure of the radiation, the mechanical responses, i.e., displacements and low-frequency vibration, can be used. For example, medical doctors already push gently and pull back to feel the static and dynamic stiffness of healing bone. To precisely analyze these responses, the displacement and vibration sensors can be incorporated at additional cost (Christensen et al., 1986; Mattei et al., 2017, 2018; Pastrav et al., 2008; Henyš and Čapek, 2019, 2018; Bediz et al., 2010; Di Puccio et al., 2017; Leuridan et al., 2017; Collier and Ntui, 1994; Ryder et al., 1993; Van der Perre and Lowet, 1996). In these procedures, the posture and the boundary conditions naturally affect

the responses of human body. For example, patients may move their legs down or up during diagnosis to relieve pain or for no reason. However, doctors should use their empirical experiences of the diagnosis of patients by hand. From the point of view of mechanical engineering, the static and dynamic response varies depending on the boundary conditions and body posture. Therefore, it may be necessary to quantitatively investigate the effect of the boundary conditions on the dynamic responses.

This paper studies the experimental diagnosis methods considering some boundary conditions in order to diagnose fractures and osteogenesis imperfection using low-frequency transverse vibration in Table 1. As the pose of human varies, the boundary conditions affecting the transverse vibration become different from a mechanical engineering

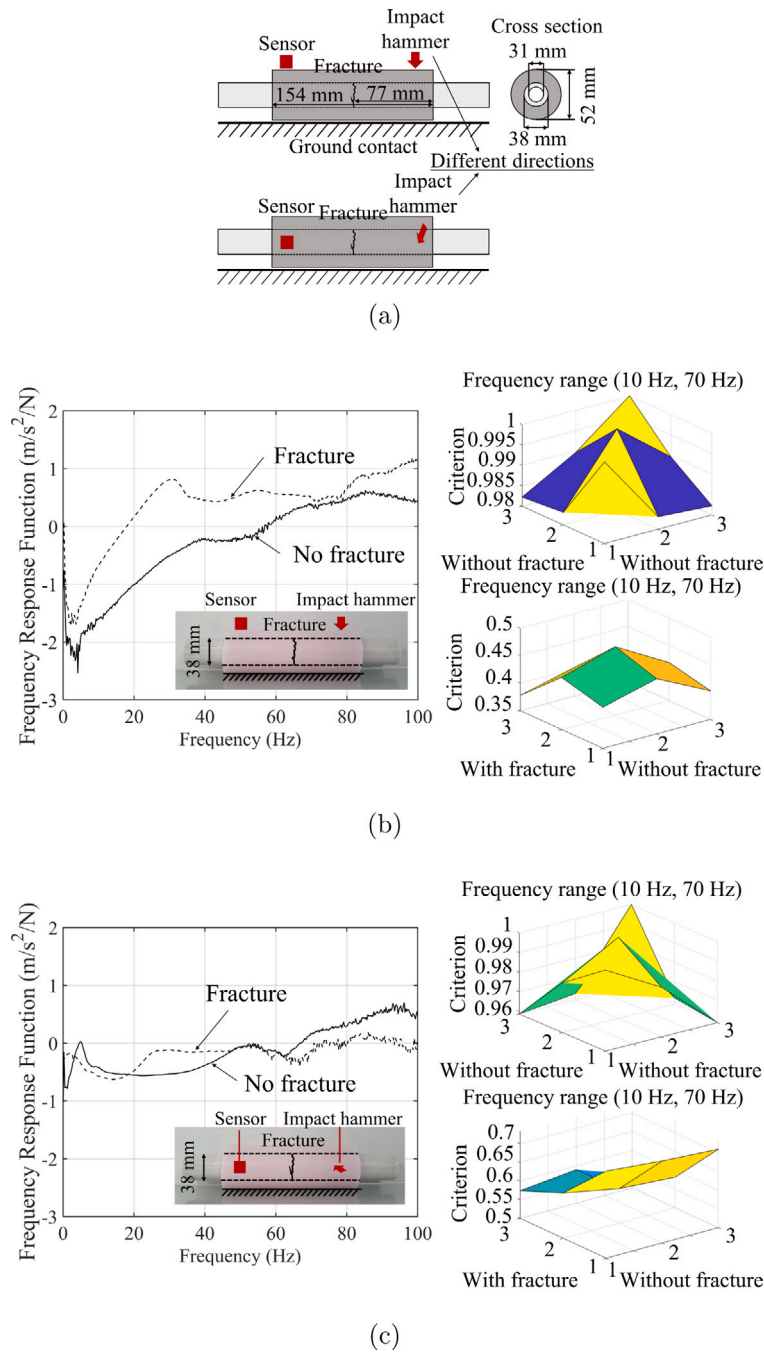


Fig. 4. Vibration tests for the effect of the size of bone with plastic bar and silicon. (a) Thicker plastic bars and silicon specimens (38 mm and 31 mm for the outer and inner radii), (b) the responses to the vertical direction load and (c) the responses to the horizontal direction load.

Table 1

The three boundary conditions considered in the present study.

Boundary condition 1: the direction of the impact force
Boundary condition 2: the varying thickness under foot
Boundary condition 3: the variation of knee angle

point of view. The differences in the responses in the frequency domain considering the boundary conditions contain valuable information regarding the stiffness and strength of specimens. Indeed, the diagnosis using transverse vibration data should consider the effect of the boundary condition. In order to distinguish these differences according to person's posture, the transverse vibration experiments with several cases of boundary conditions, i.e., lay-down, standing up and sitting,

are carried out. After measuring the vibration data with the different boundary conditions, the numerical decision algorithm using the virtual spectrogram is applied to identify the existence of crack. To validate the present approach, several experiments are carried out with plastic bars with silicon, animal legs and a cadaver. After integrating all key technologies, a smart diagnosis system, as shown in Fig. 1, was extended.

The remainder of this paper is arranged as follows: Section 2 provides an overview of the phenomena of bone fracture. Experimental results obtained using artificial specimens, animal legs, and a cadaver are presented. Experimental results including a cadaver test are presented to investigate the effect of the boundary conditions in Section 3. The conclusions and findings are summarized in the conclusion.

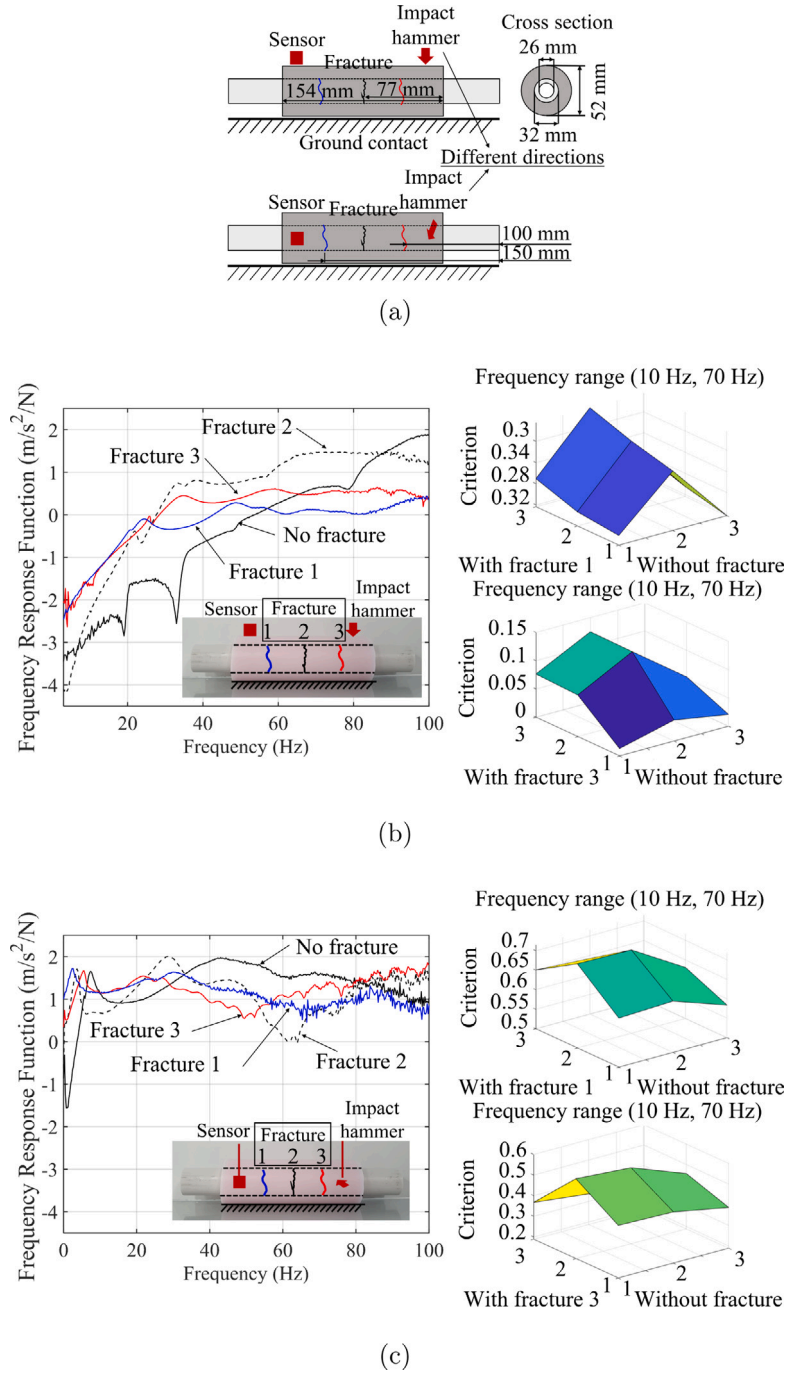


Fig. 5. Vibration tests for the effect of the different locations of fracture with plastic bar and silicon. (a) Plastic bars and silicon specimens, (b) the responses to the vertical direction load and (c) the responses to the horizontal direction load.

2. Transverse vibration considering boundary condition

2.1. Bilateral symmetry and smart diagnosis system with the Modal Assurance Criterion (MAC)

The bilateral symmetry plays an important role in the present study. To have a reliable reference, the use of the bilateral symmetry was proposed (Yoon et al., 2021; Jacob and Wyawahare, 2013). Indeed, this research also adopts the application of the bilateral symmetry. This study presents the application of the bilateral symmetry and the effects of the boundary conditions are considered. In addition, it is also proposed that the MAC value can be utilized to diagnose the existence of fracture with several boundary conditions.

The classification is carried out based on the modal assurance criterion (MAC) in (1). To investigate the robustness of the system, the present approach investigates the characteristics of the signals in the frequency domain. To achieve this purpose, the frequency range of the curve for the evaluation of ϕ in (1) should be determined in prior. This research sets the maximum frequency value in the range of 60 to 100 Hz. With this choice, the criterion algorithm shown in Fig. 2(b) can be developed. The maximum reference value of the MAC can be determined by experiments considering the three boundary conditions.

$$\phi = \frac{|\mathbf{X}_{\text{No fracture}} \cdot \mathbf{X}_{\text{Signal}}|^2}{|\mathbf{X}_{\text{No fracture}}|^2 |\mathbf{X}_{\text{Signal}}|^2} \quad (1)$$

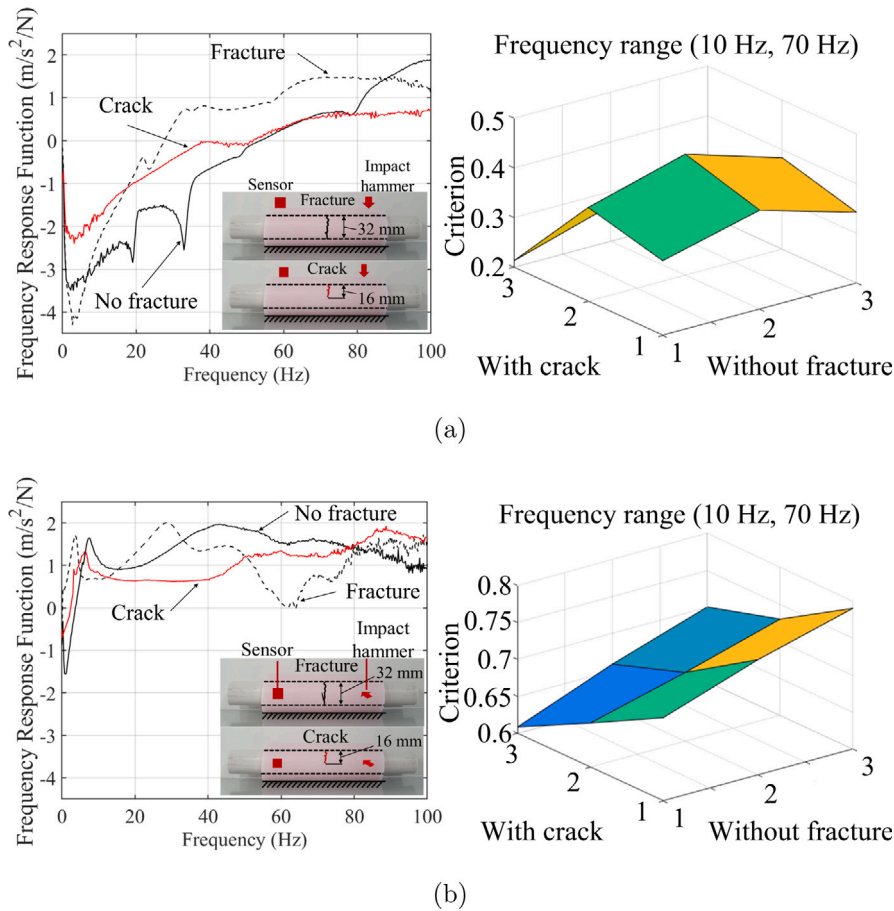


Fig. 6. Vibration tests for the effect of the different sizes of fracture and crack with plastic bar and silicon. (a) The responses to the vertical direction load and (b) the responses to the horizontal direction load.

The reference signal, $\mathbf{X}_{\text{No fracture}}$, is the signal without fracture, and the measured low-frequency vibration signal is denoted by $\mathbf{X}_{\text{Signal}}$. The frequency response functions through the vibration based impact experiment with normal or fractured bone are denoted by $\mathbf{X}_{\text{Signal}}$. Considering the effects of the boundary conditions, the criterion values, ϕ^* , are determined.

$$\begin{cases} \phi \geq \phi^* & \text{No problem (No fracture or no degenerative bone)} \\ \phi < \phi^* & \text{Problem (Fracture or degenerative bone)} \end{cases} \quad (2)$$

where the critical value separating signals is denoted by ϕ^* . The criterion value is determined heuristically. The concept of the MAC value in (2) means that in case of one or near one for the MAC value, it indicates that two signals are similar. A lower value for the MAC indicates that the two signals are different.

2.2. Experimental methodology (single input and single output) and materials

To investigate the effects of the boundary conditions, this study conducts experimental studies on plastic bars and silicon, artificial bone and cadaver with the three boundary conditions mainly affecting the transverse vibration of the specimen. To investigate the effects of the boundary conditions on the transverse vibration responses, several experimental studies are carried out with plastic bar and silicon, artificial specimen and the cadaver specimen. In this study, the material properties of the plastic pipe and silicon are set as follows: (Silicon: $\rho = 1500 \text{ kg/m}^3$, $E = 1 \text{ MPa}$, $\nu = 0.47$; plastic pipe: $\rho = 1330 \text{ kg/m}^3$, $E = 2 \text{ GPa}$, $\nu = 0.4$) and artificial bone is made with almost the similar material properties as real human bone (artificial bone: $\rho =$

2000 kg/m^3 , $E = 2.13 \text{ GPa}$, $\nu = 0.3$). For gelatin, ballistic gelatin coagulated by mixing gelatin powder with water is used and it is known that ballistic gelatin has the material properties very similar to those of human or animal muscles.

In this study, two specimens with and without fracture were prepared and tested at least 3 to 10 times to calculate the average responses of these data. Not to mention, the transverse vibration data analyzed in the smart diagnosis system are dependent on the boundary conditions as well as the applied force. An impact hammer is employed in order to apply the force with an accelerometer sensor measuring the acceleration. Low-frequency vibration signals were recorded using a DAQ device. It is important to maintain the locations of sensor and impact hammer for consistent measurement in vibration-based approach. From our experiment, it is observed that reliable vibration data from 10 Hz to 100 Hz range can be obtained but influenced by the boundary condition. The signal processing with fast Fourier transform (FFT) is performed to analyze the data. The vibration-based mechanical approach has the advantages of being inexpensive, lightweight, non-invasive, portable, non-radiative, and capable of being used in underdeveloped environment. For the experiments, the accelerometer (PCB 352C33) and the hammer (PCB 086C03) are used with a NI-9234 DAQ device for the data acquisition.

3. Experiment results and discussions

3.1. Effect of the direction of impact force (horizontal or vertical load)

First of all, this subsection considers the effect of the direction of the impact impulse force (Leonard, 1986). The magnitude of the impact

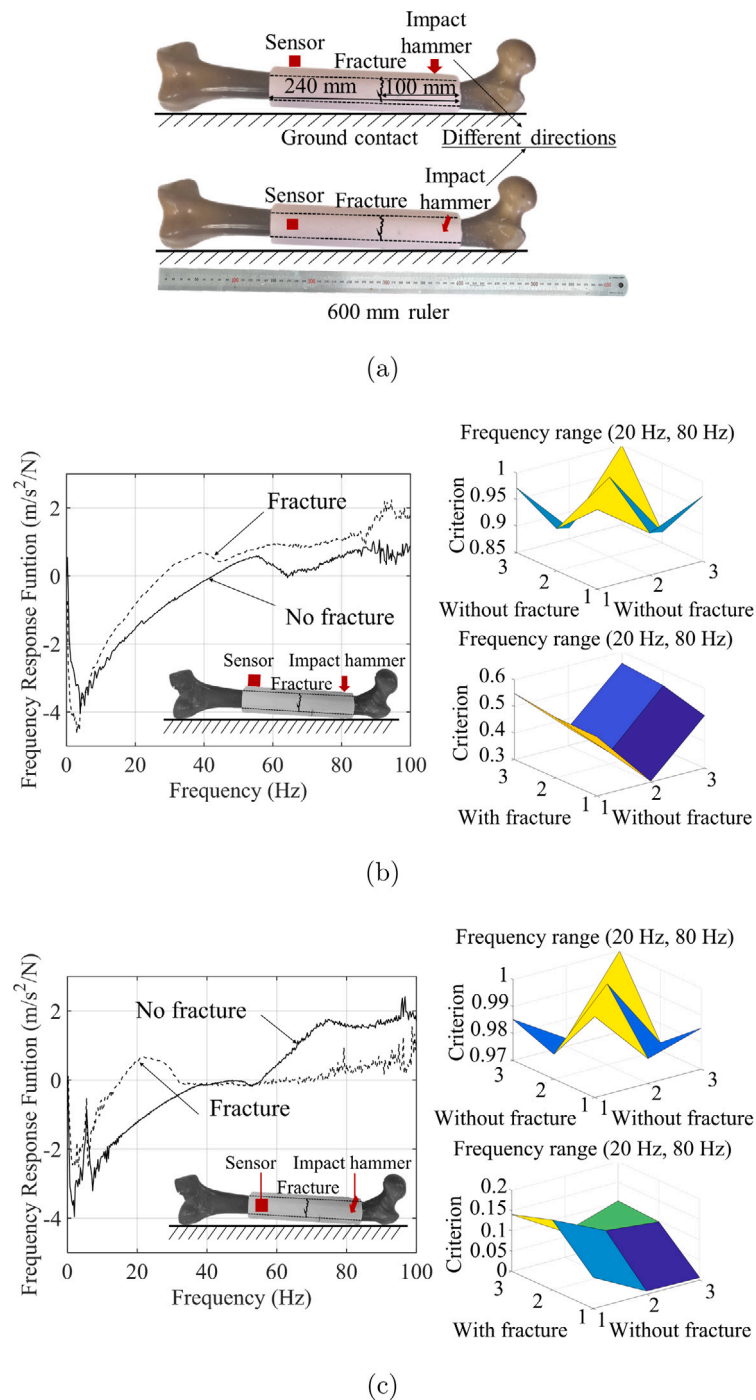


Fig. 7. Experiments with artificial bone and silicon. (a) Artificial bones and silicon specimens, (b) the responses to the vertical direction load and (c) the responses to the horizontal direction load.

force is between 1 N and 8 N which does not cause discomfort to the patient. Not to mention, the transverse vibration data vary depending on the direction of the impact force. The amplitudes and frequencies of vibration data depend on the direction of the applied impact force, which affects the accuracy of smart diagnostic systems. The present study suggests to utilize the bilateral symmetry to determine the threshold value. For example, it is possible to diagnose the condition of right leg with the information of left leg in a normal condition. With the signal of the normal condition in advance, it is also possible to diagnose the status of bones. For example, Fig. 3 shows the transverse vibration data depending on the location and direction of the impact

force. In Fig. 3(a), the condition at which patient is positioned in long-sitting on bed and legs is assumed and the substitutes are put on the ground and the vertical and the horizontal impact forces are applied in Fig. 3(b) and (c), respectively. Interestingly the frequency response functions are very different for the same specimens with respect to the different force directions. In Fig. 3(b), the amplitude of the responses of the fracture specimen is higher than that of the unfractured specimen. Below 10 Hz, the response of the unfractured specimen is higher due to the boundary condition and until 90 Hz, the amplitudes of the responses of the fracture specimen are higher. With the utilizing these features, it is possible to diagnose whether a specific

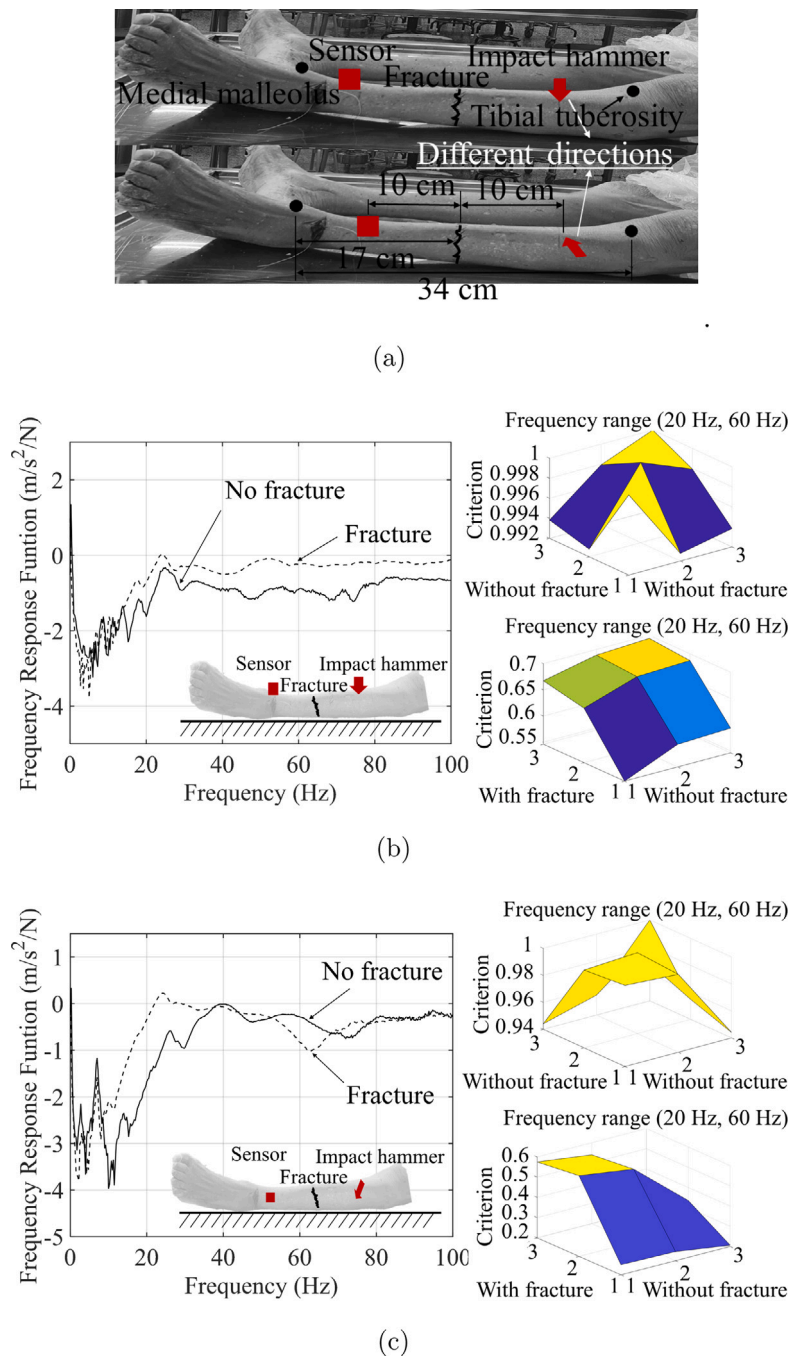


Fig. 8. Experiments with cadaver. (a) Cadaver specimens, (b) the responses with the sensor and the actuator attached to the vertical direction load and (c) the responses with the sensor and the actuator attached to the horizontal direction load.

specimen is fractured or not fractured. Note that this research considers the amplitudes over the frequency domain in addition to the resonance frequencies. The MAC values are calculated with the data sampled by the three tests for each case in Fig. 3(b:right). The similarities among the data are determined. For example, the MAC values computed with the transverse vibration data without fractures are over 0.95 and the MAC values computed with those of fractured and unfractured specimens become lower than 0.5. These differences are escalated further by adjusting the frequency range and this research adopts the frequency range between 20 Hz and 80 Hz. Fig. 3(c) shows the vibration data with the horizontal direction force and the acceleration in the same direction is also measured. The overall amplitudes become higher than those in Fig. 3(b) as the direction of the force are physically perpendicular to the

boundary condition. As opposite to the vibration case of Fig. 3(b), the average amplitudes of the fractured specimen are lower in Fig. 3(c). The changes of the magnitudes are observed below 40 Hz. The MAC values of these vibration signals are also applicable in separating the signals and the features in Fig. 3(b) and (c) can be implemented in a smart diagnosis system. One thing what we want to emphasize is that the transverse vibration data without fracture should be presented as a reference signal and can be obtained by the usage of the bilateral symmetry. It is also an issue about the applicability of the present approach with the vibration on the diagnoses of various fractures. Thus, several experiments with different size of bones, different locations of fracture and different size of fractures are carried out. The experimental results show that it is possible to apply the frequency response function

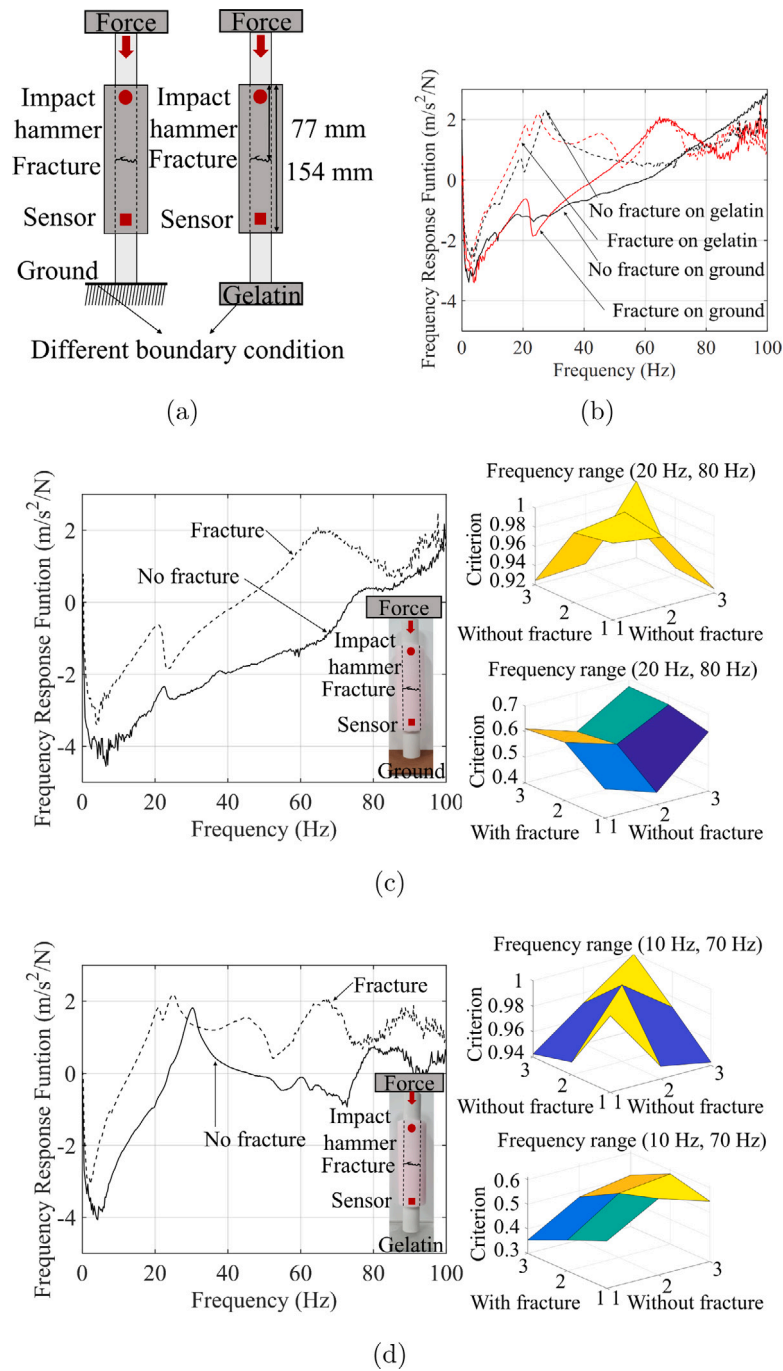


Fig. 9. Compare without fracture and with fracture. (a) Gelatin specimens with and without elastic foundation (Force : 11.76 N), (b) transverse vibration signals, (c) vibration signals without elastic foundation, and (d) vibration signals with elastic foundation.

for the different situations. With the different size of bones, the MAC values with and without fracture show sufficiently different values in Fig. 4. In Fig. 5, the effect of the fracture location is tested. This shows that the MAC values are sufficiently different. Fig. 6 investigates the effect of the size of fracture. Unlike the other cases, there are small differences in the responses.

In order to improve the similarity toward human bone and muscle, the artificial bone whose materials are known to be similar to those of human is experimented with the same conditions in Fig. 7. The transverse vibrations before and after fracture are measured by varying the direction of the impact force too. Fig. 7(b) and (c) show the frequency responses of the vibration data of these experiments. These curves illustrate that the responses of the artificial bone with silicon

in Fig. 7 are similar to those of the plastic bar with silicon in Fig. 3 and can be used as substitutes in order to investigate the vibration features of human. Due to the degeneration of stiffness with fracture, the resonance peaks observed between 20 Hz to 100 Hz appear in lower frequency domains compared with the resonance peaks of healthy specimens for both vertical and horizontal impacts. This aspect offers practical importance as the use of human specimens is limited in terms of quantity and quality. In other words, it is possible to stack the relevant data regarding various fractures with the artificial plastic bars.

In order to distinguish the above signals, it is possible to apply the MAC in (1). Considering the observations in the precedent researches and the above responses, this research suggests to use the transverse

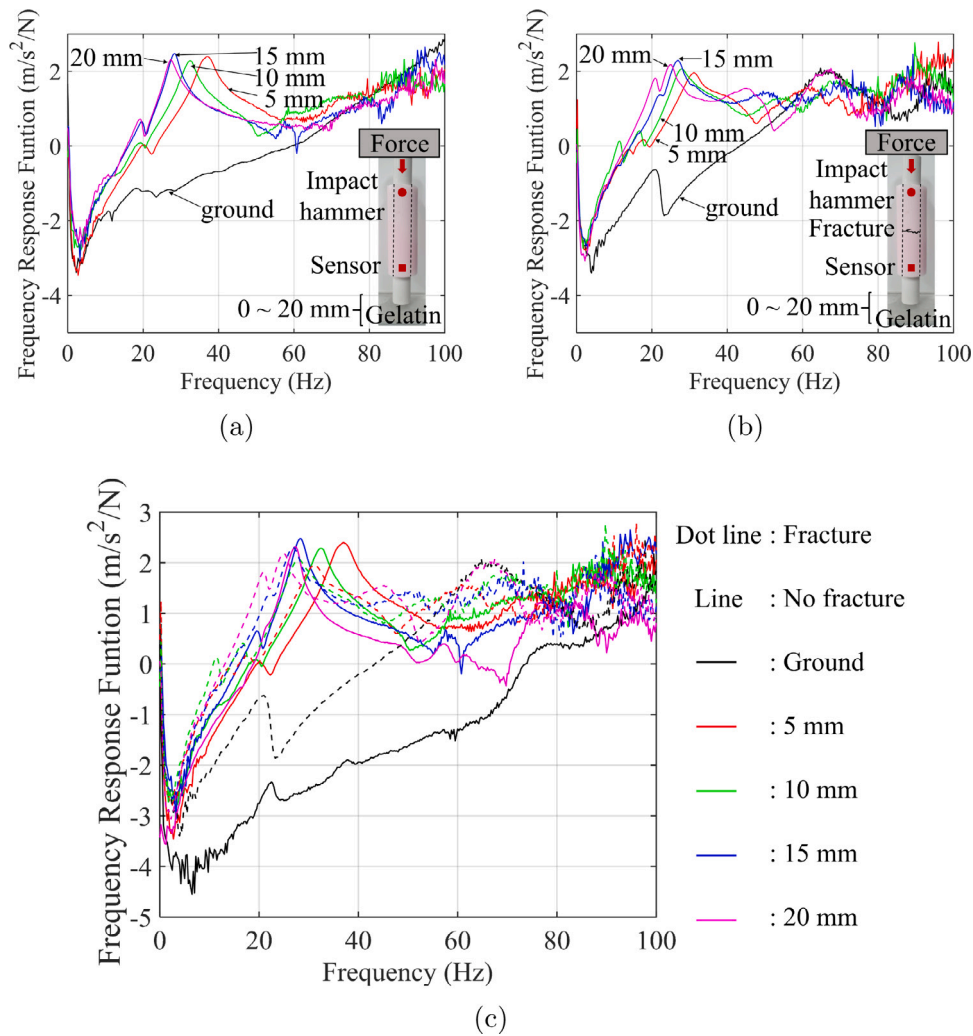


Fig. 10. Transverse vibration data with various elastic foundations. (a) Data without fracture, (b) data with fracture and (c) data without fracture and with fracture.

vibration signals below 100 Hz. Depending on the experimental conditions, the critical value of the MAC should be chosen. The above figures illustrate the curves of the MAC values for several specimens with and without fractures. The responses of the bone without fracture are set to the reference signals. Based on these results, this study proposes to adopt a real value between 0.4 and 0.5 for the MAC value. The values larger than the critical value indicate consistent correspondence whereas small values may indicate poor resemblance of two signals and imply potential fractures. In short, the observed MAC value can be used to identify whether a bone has fractures or not.

For a final verification, the above experiments are repeated with a cadaver (male, 84 years old, 168 cm tall) in the anatomy laboratory in Hanyang University, Seoul, Korea, on July 2020. The tibia on one side of the body was fractured and the body was laid on a table. The bone fracture was made on the midpoint between the tibial tuberosity and the medial malleolus using a bone saw. The vertical or horizontal impact forces are applied and the accelerations are measured and analyzed with the same approaches above. Fig. 8 shows the experiment setup in (a), the analysis with the vertical force in (b) and the analysis with the horizontal force in (c). The responses are similar to those observed in the plastic pipes and the tailored bone substitute. Again the frequency domain is set from 20 Hz to 80 Hz due to the uncertainty of the boundary condition. It is important to consider the material properties of bone such as Young's modulus, porosity and density. From a mechanical engineering point of view, with a bone with a lower density, the resonance frequencies become different with

lower amplitudes; the ratio of the stiffness to the mass determines the resonance frequencies. Therefore, the concept of the bilateral symmetry can be employed.

3.2. Experiments with gelatin foundation

For a next experiment, plastic pipes with elastic foundation are considered in Fig. 9. The objective of this experiment is to investigate the effect of the elastic boundary condition. The transverse vibration data for the impact force applied perpendicularly to the pipes are measured to identify the existence of fracture as shown in Fig. 9(a). Fig. 9(b) shows the detailed vibration data in our experiment. The responses with red color are the responses with fracture where the responses with black color are the responses without fracture. It is observed that the amplitudes between 10 Hz to 80 Hz with the gelatin substrate become larger. In order to separately investigate these data, Fig. 9(c:left) shows the transverse vibration data with and without fracture for the grounded artificial pipe. Here it turns out that the amplitude of response without fracture becomes larger. For the robustness, the three experiments are carried out for each case and Fig. 9(c:right) shows the MAC values from 20 Hz to 80 Hz of these experiments. The frequency domain is chosen to remove the oscillating signals below 20 Hz and over 80 Hz. As illustrated, the criteria with the MAC can be used to distinguish the cases. In Fig. 9(c and d), the MAC values above 0.9 are obtained with the data with fracture and the MAC values below 0.7 are obtained with the fracture and non-fracture

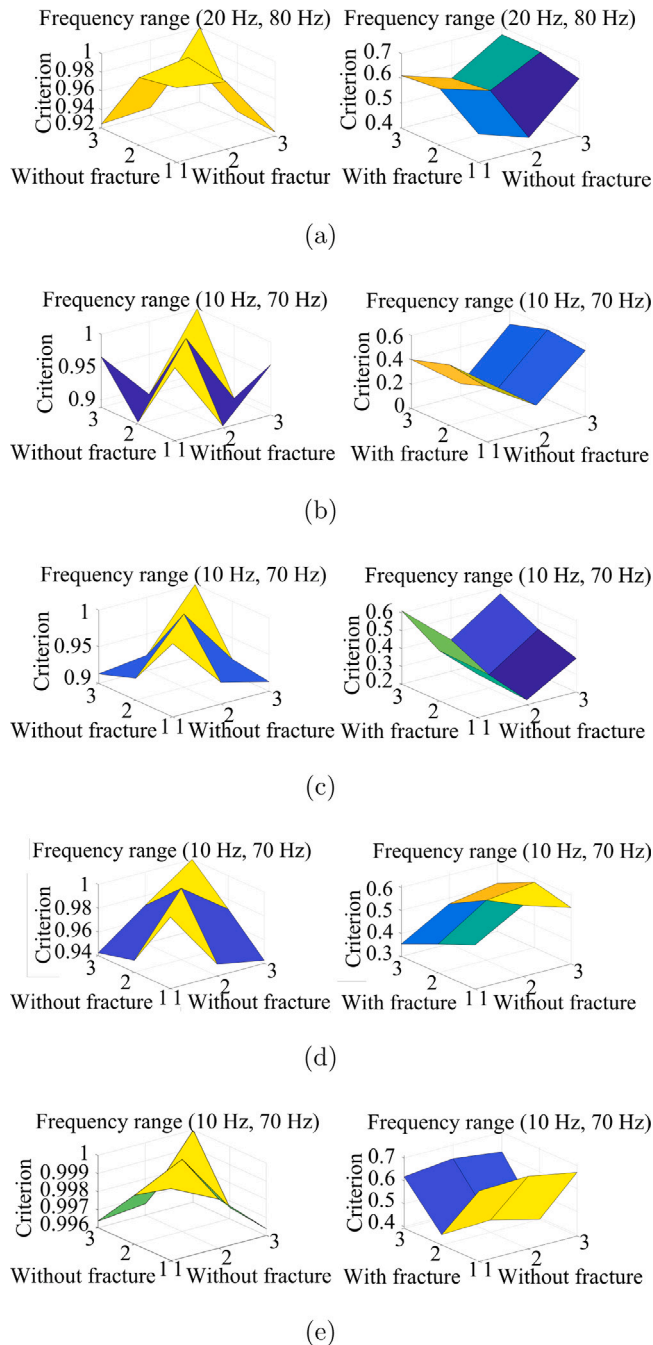


Fig. 11. Modal assurance criterion with and without elastic foundations. (a) MAC without elastic foundation, and (b–e) MAC values with various elastic foundations (b: 5 mm, c: 10 mm, d: 15 mm and e: 20 mm).

signals. Fig. 9(d:left) shows the experimental data with the 15 mm thickness gelatin foundation. Due to the stiffness of the gelatin layer, the resonance peak around 30 Hz appears. The resonance frequency around 30 Hz after fracture illustrates that the interpretation of the simple spring–mass vibration can be possible. Fig. 9(d:right) shows the MAC values. Similar to Fig. 9(c:right), it turns out that the MAC based identification method can be an efficient measure in these cases. With the elastic foundation, the frequency domain between 10 Hz to 70 Hz is chosen. Comparing with Fig. 9(c) and (d), it is recognized that the elastic boundary condition is important in the vibration data. Being impossible to make the cadaver upright position, we failed to carry

out and verify the experiment with several elastic foundations with the cadaver.

Fig. 10 shows the frequency response functions with the various elastic foundation, i.e., 5 mm to 20 mm in 5 mm increments, with the 11.76 N force. By changing the thickness value of the gelatin elastic foundation, the variations of the frequency responses function are observed with or without fracture. The stiffness and resonance frequency become lower by increasing the height of the gelatin foundation. Note that the stiffness of the elastic foundation is inversely proportional to the height and the increase of the thickness higher the resonance peak. These response changes can be quantified as the representative MAC values and can be used to determine the presence or absence of cracks with the elastic foundation in Fig. 11.

3.3. Experiment concerning knee angle

For a final experiment, the effect of knee angle on signals is considered. The objective of this experimental study is to find out an optimal knee angle to classify the status of bone. Two plastic bars coated silicon layers are linked as shown in Fig. 12(a). By varying the angle between the plastic bars with the clamped side, the accelerations with and without fracture are measured in Fig. 12(b: without fracture) and (c: with fracture). The responses show the complex dependency with respect to the specified knee angle. Thus it's challenging to say quantitatively what angle is best to differentiate these data. Having investigated and studied these data in Fig. 12(b) and (c), it is found that 90 degrees of the knee angle is the best angle to distinguish these vibration data with or without fracture. See Fig. 12(d) showing the vibration data with 90 degrees for the knee angle. The distinct differences are observed around 30 Hz. The transverse vibration data without fracture is lower than that with fracture at these frequencies. This implies that the transverse vibration data with this 0 degrees angle can be utilized in a smart diagnosis system. The right column of Fig. 12(d) shows the MAC values with these data; the three experiments are carried out with and without fracture and these data are analyzed to compute the MAC value. The upper value around 0.9 can be used to separate these data with and without the fracture using the modal assurance criterion. In addition to these experiments, a cushion is placed underneath the specimens as often patient's legs are placed over the cushion during medical diagnosis in Fig. 13. From a mechanical point of view, this cushion can be regarded as the visco-elastic support which increases the complexity of the signals. With a normal cushion, fortunately its effect is not significant investigated in our research and the responses and the MAC values between 20 Hz and 100 Hz are similar to those without cushion. Note that in Fig. 13(b), the sensor and the impact hammer are located vertically where in Fig. 13(c), they are located horizontally. The responses are varied depending on the direction of the force as observed in the previous experiments. The resonance peak and responses around 30 Hz in the cushion with the fracture-free specimen are equal to the resonance and responses near 50 Hz without the cushion specimen. The resonant peak about 50 Hz without cushion is equivalent to the resonance peak about 90 Hz with no crack and cushion. In our experiment, it is also observed that the noises are smaller in the experimental setup with the horizontal force and sensor in Fig. 13(c). This can be explained by the contact condition between the specimen and the cushion. In other words, compared with the vertical configuration in Fig. 13(b), the effect of the cushion is minimized with the configuration in Fig. 13(c). This aspect is also observed in Fig. 3. In short, depending on the directions of the sensor and the force, some differences are observed. When the reference signals are adequate, the MAC can be used to distinguish the signals. It was tried to use a cadaver to check this feature. However, the varying the knee angle in a cadaver is impossible as the treatment of a corpse makes joint stiffness in our experiment. It is our limitation that this study should be verified with living peoples in future.

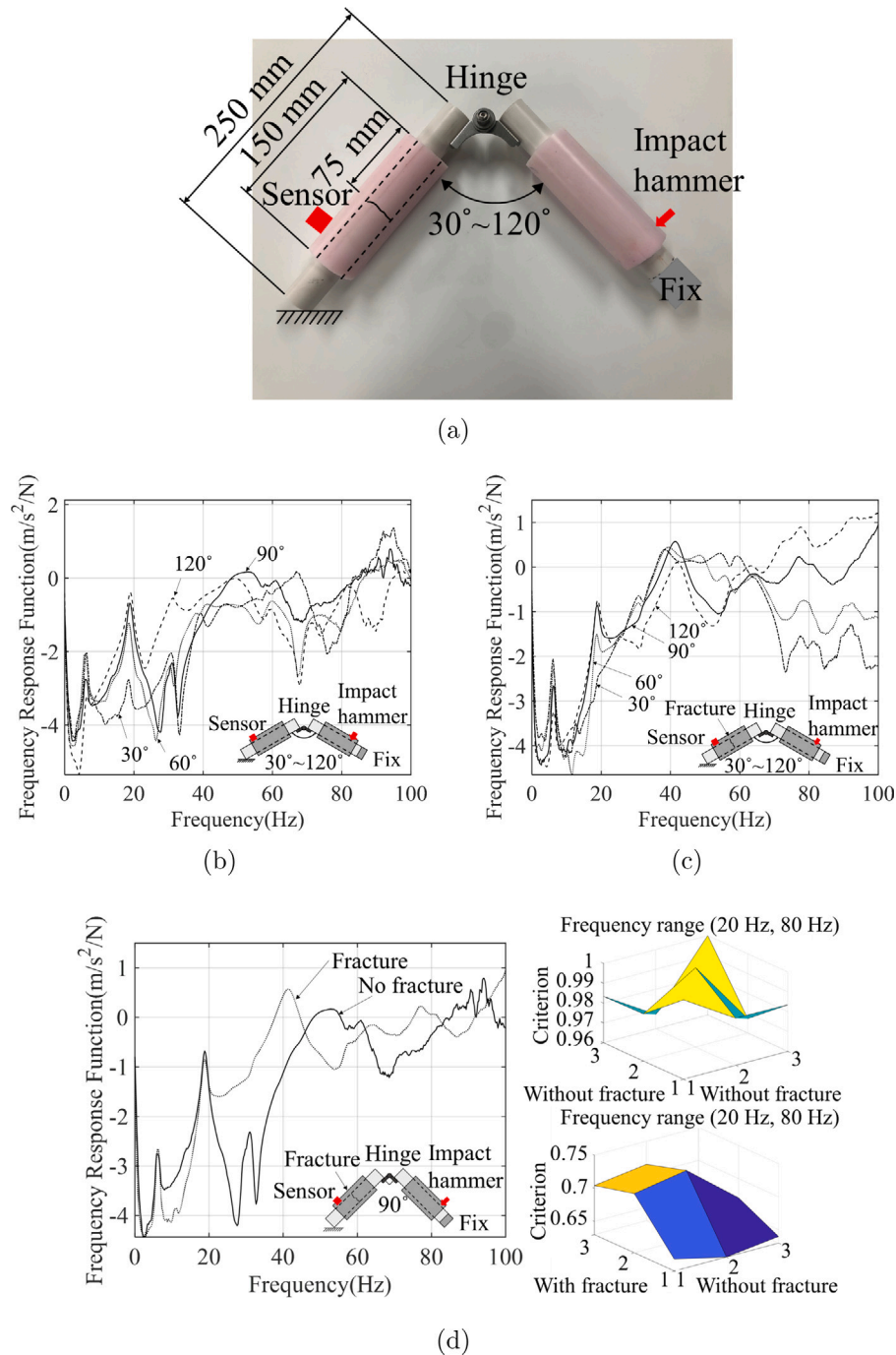


Fig. 12. Experiment for knee angle. (a) The experiment status, (b) the transverse vibration data without fracture for various knee angles, (c) the transverse vibration data with fracture for various knee angles and (d) the vibration data with 90 degrees.

4. Conclusions

This experimental study provides a new insight into the effect of the boundary conditions on fractured human vibration. Medical doctors faced difficulties in reliably and frequently identifying the damage and modal parameters of patients as they are time varying vibration data due to the time varying material properties and their postures (boundary conditions). In order to investigate the effect of the boundary conditions, this study conducts experimental studies on plastic bars with silicon, artificial bones and cadaver with the three boundary conditions mainly affecting the transverse vibration of the specimen. To investigate the effects of boundary conditions on the transverse vibration, several experimental studies are carried out here with plastic

bars with silicon, artificial specimens and the cadaver specimen. In order to investigate the existence of fracture, it is ideal to conduct the experiments in the plane ground condition with horizontal load. Being often difficult to carry out the experiment with the ideal boundary and loading condition, the boundary conditions and the loading condition should be considered. In order to categorize the transverse vibration data, the criterion based on the modal assurance criterion (MAC) is applied and it turns out that the MAC values at the low frequency domain provide information to answer the foregoing fracture question considering the boundary conditions. In summary, the present research conducts an experimental study in order to enhance the accuracy of the smart diagnostic system based on the transverse vibration data at a low cost.

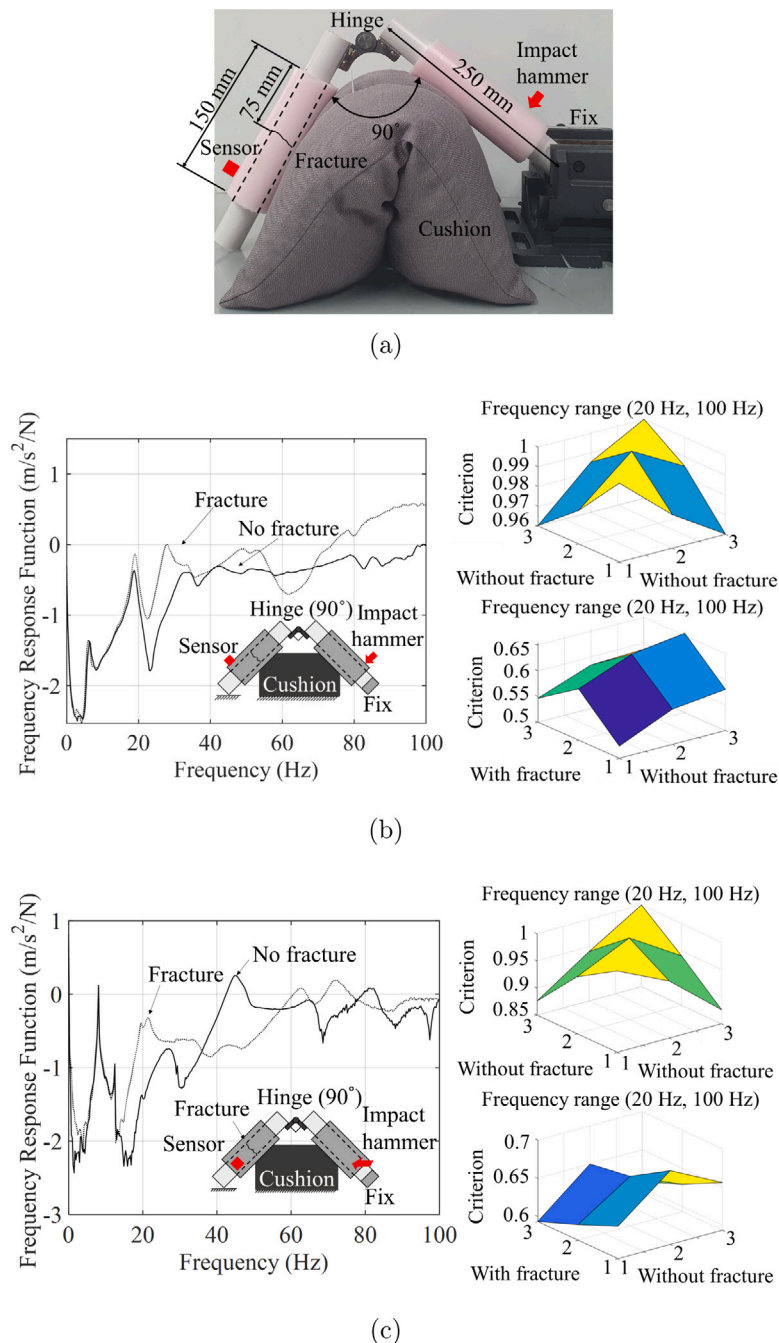


Fig. 13. Experiment for knee angle with cushion underneath. (a) The experiment status, (b) the responses with the sensor and the actuator attached to the vertical direction surface of the knee angle and (c) the responses with the sensor and the actuator attached to the parallel direction surface of the knee angle.

CRediT authorship contribution statement

Seong-Gyu Sim: Prepared the specimens and carried out the experiment. **Yeon-Jun Woo:** Prepared the specimens and carried out the experiment. **Dong-Yoon Kim:** Prepared the specimens and carried out the experiment. **Se Jin Hwang:** Prepared the specimens and carried out the experiment, Wrote the manuscript, Helped supervise the project. **Kyu Tae Hwang:** Wrote the manuscript, Helped supervise the project. **Chang-Hun Lee:** Wrote the manuscript, Helped supervise the project. **Gil Ho Yoon:** Wrote the manuscript, Conceived the original idea and supervised the project.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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