A novel design of rat’s head positioner for MRI and its feasibility

Hirohisa NARITA* and Masayuki YAMADA **
*Department of Mechanical Engineering, Faculty of Science and Technology, Meijo University
1-501 Shiogamaguchi, Tempaku, Nagoya 468-8502, Japan
E-mail: hnarita@meijo-u.ac.jp
** Faculty of Radiological Technology, School of Health Sciences, Fujita Health University
1-98 Dengakugakubo, Kutsukake-cho, Toyoake, Aichi 470-1192, Japan

Abstract
A novel design of an animal bed, which is termed “head positioner”, for fixing a rat is newly proposed in this research. The head positioner is used for a basic medical study to analyze brain activities for small animals with MRI (Magnetic resonance imaging). Various requests and specifications for it is described by investigations and our preliminary experiments in advance. A rat’s head positioner is designed by a 3D CAD (Computer Aided Design) and also created by a 3D printer with using PLA (polylactic acid) resin. An MRI experiment is performed by the new head positioner and a lot of sharp images can be taken by reducing a rat’s head motions. The images of the rat’s brain data can be also taken with the same angle as a brain Atlas which combine geometric positions with brain functions in a form of geography. It enables us to analyze the rat’s reaction from the viewpoints of the brain functions. A feasibility of the new design of rat’s head positioner is demonstrated in this paper.

Keywords: Design, Head positioner, Rat, MRI, Brain atlas, 3D printer

1. Introduction
Translational MRI (Magnetic resonance imaging) research with using rodent models are indispensable in many basic medical researches (Hansen et al., 1980)(Denic et al., 2011)(Tanoue et al., 2015), because it is a non-invasive monitoring device. Many MR-images of a small animal model’s brain taken by MRI are generally examined with reference to the Atlas (Paxinos, G. and Watson, C., 2013), which describes functions and geometric positions of the brain tissue in a form of geography.

A head positioner, which strongly fix a small animal’s head with consideration of the head shape, is required to reduce disturbances of the taken images such as bulk-motion as much as possible, because it takes a lot of time to have MR-images on its brain. The images of its brain must be also taken with a same angle as the Atlas in order to discuss accurate its brain activities. A rat, which is a typical rodent, is treated as the small animal model in this research. Figure 1 (a) shows a conventional rat’s head positioner which is attached to MRI, originally. The rat is fixed by only its front teeth, hence this cannot fix the rats rigidity, and the rat’s head rotates around an axis line of the bed curve. Figure 1 (b) shows another conventional rat head positioner made by PMMA (Polymethyl methacrylate) pipe. This kind of the head positioner has been developed by each researcher. The rat is fixed by hanging its front teeth and pulling its head. The bulk-motion occasionally appear in the taken images and the brain angle is not same as the Atlas.

Hence, several specifications required for a rat’s head positioner is revealed and a novel design of the rat’s head positioner is newly proposed in order to solve the aforementioned problems in this paper. The rats used for MRI examinations is almost same shape, hence the designed head positioner can be applied to other rat. The new head positioner is created by a 3D printer and a feasibility of the designed head positioner is demonstrated through an MRI imaging experiment. The design of the head positioner has not been discussed in detail from the viewpoints of mechanical engineering so far, this is an important and a unique approach to support the basic medical researches.
2. Manufacturing process of rat’s head positioner

2.1 Manufacturing flow

Figure 2 shows a manufacturing flow of rat’s head positioner. The DICOM (Digital Imaging and COmmunications in Medicine) (Kahn et al., 2007) data of a rat is obtained by CT (Computed Tomography) in advance. The DICOM format is a world standard as a matter of practice for storing, printing, and transmitting information regarding medical imaging. The DICOM data consists of a patient’s images and many attributes such patient name, sex, age and so on. A target rat’s head shape is detected from all images of DICOM data.

A 3D (3-dimentional) virtual model is generated based on the detected shape. The head positioner is designed with consideration of the 3D rat’s head virtual model and limited small imaging space of MRI. A physical 3D model is created by a 3D printer based on a generated stl (STereo Lithography) file after designing the head positioner. Some MRI experiments are carried out by setting another rat to the head positioner for evaluating its performance.

2.2 3D virtual model generation for a rat’s head

The DICOM data includes a lot of images at regular intervals of several milli-meters. Monochrome shades generally appear in the images according to various signal strengths. For example, the signal strengths of water, bone and metal corresponds with 0, 1000 and 4000 for CT number (Hounsfield unit) (Brooks, 1977). The window level and the window width (Ernst et al., 2002) must be decided with viewing monochrome images of the rat’s head in order to see all images on a screen as shown in Fig.3. The window level and window width mean a center value of a range of the CT numbers.
displayed and a range of CT numbers in which an image contains, respectively. In other words, grey level values of a screen must be decided. The maximum and minimum thresholds of the signal strength on the images to detect a target object are determined after deciding the window level and the window width. Figure 4 (a) shows the detected points (signal strength) on an image data. Iso-surface (Labsik et. al., 2003), which corresponds a surface representing points of constant signal strength, is generated from all images. Figure 4 (b) shows the generated virtual 3D model of the rat’s head. There are a lot of vertexes for the 3D virtual model, hence the vertexes are reduced to 20% in order to output stl data after eliminating unnecessary parts. Figure 4 (c) shows the output stl data of the rat’s head. DeVIDE (Botha and Post, 2008), which is an open source software framework, is applied to realize the aforementioned process. The design of the head positioner is carried out by importing the stl data of the rat’s head.

Figure 2 Manufacturing flow of rat’s head positioner

Figure 3 Window level and window width

Figure 4 Detected rat’s shape from DICOM image data
2.3 Design and creation of the head positioner

2.3.1 Required specifications

The disturbance tends to occur in the MRI examinations due to the rat’s body motion, because it takes a lot of time. Experimenters in medical research are also difficult to compare both MR images and the Atlas, when the angle between the images obtained by MRI and the Atlas differs. In addition, the rat’s head must be fixed in a solenoidal coil, whose diameter is 38.5 mm, because some devices and some lead wires are set to the rat for monitoring vital signs during an operation. The diameter of the solenoidal coil is very small and operability must be considered, hence we cannot apply the sophisticated shape and must realize the simple design.

The specifications required for the head positioner becomes the followings due to some preliminary discussions and various preliminary experiments.

1. A base of front teeth and earholes must be arranged in alignment (or top of the head must be flat) in order to become the same angle of the Atlas.
2. The upside of the head positioner is opened to perform various operations.
3. The head positioner can be carried to the solenoidal coil while fixing the rat.
4. The head positioner can reduce the rat’s body motion with consideration of the rat’s head shape due to breathing and other motion without applying a compression on the rat’s eyes.
5. The setting time is as short as possible.
6. A tube connector whose diameter is 6 mm in order to flow anesthesia can be set to the head positioner.
7. The rat’s forefoot should be released to avoid a cramped situation.

2.3.2 Design

Figure 5 shows the designed head positioner drawn by a 3D-CAD (Computer Aided Design): SketchUp Make (Trimble Inc., 2017).

It consists of five parts: a bed, an incisor bar, a head cover, a guide and a cylinder hollow. The bed supports the downside of the whole body. The incisor bar, whose tip has 4.5-degree angle, hangs the front teeth by its hole. The head cover restrains the head from the above. The guide connects the solenoidal coil to slide the bed. The cylinder hollow connects the head part of the bed and the head cover.

The head cover is opened to perform various operations described in the required specification 2. A hole, whose diameter is 6 mm, is also drilled to the head cover to insert the tube connector in order to flow anesthesia described in the required specification 6.

The bed can be carried from a workbench to the solenoidal coil while fixing the rat described in the required specification 3. The head cover is separated from the bed, because it is easy to set the rat. As a result, the setting time becomes short described in the required specification 5. The front of both side walls of the bed is eliminated in order to get out of the way of the rat’s forefoot described in the required specification 7.

3-point fixation is generally applied to fix an object rigidity, however this is very difficult for the rat in MRI and also repetitive accuracy of setting the rat is not maintained. Several fixing methods have been proposed and tried for laboratory rats over and over again so far. Finally, the front teeth are hanged forward by the incisor bar and the rat’s cheeks are held by a tapered face in this research. Figure 6 focuses the head part of the bed. The tapered shape is generally applied in order to enhance a part’s rigidity (Tsutumi et.al., 1985). This kind of tapered shape is applied in order to fix rigidity and guide the rat’s head properly in this research. This is an original fixing concept to realize the rigid fixation of the rat’s head and repetitive accuracy of setting the rat, simultaneously. As the result, anyone eliminate the rat’s head motion and set the rat with the same angle of the Atlas any time. The required specifications 1 and 4 are realized by the incisor bar and the tapered face.

The tapered shape is made by 18, 22, 27, 32 and 34 mm-diameter from the rat’s nose tip at 10 mm intervals. This tapered shape is determined by applying an envelope surface of the rat’s head with maintaining the same angle of the Atlas and unwanted surface parts are eliminated from the envelope surface. This head part also hold the rat’s neck firmly without squeezing the rat’s throat. Figure 7 shows a snapshot of a setting situation of the rat with hanging its front teeth.
A material of the head positioner must be a resin, because the resin is MR-compatible. The head positioner is created by a 3D printer, which is MakerBot Replicator 2 (MakerBot Industries LLC), with using PLA (polylactic acid). Table 1 summarizes operating parameters of the 3D printer. Support materials are removed by an ultrasonic cutter after creating the head positioner parts.

A mock model of a lifelike rat head has been generated by a clear polyurethane resin. A collision check between head positioner and eyeball of the rat and shape corrections have been carried out in detail with using the mock model.
Table 1 Operation parameters of a 3D printer

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<td>Layer Height (mm)</td>
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<td>Feed rate (mm/s)</td>
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<td>Print temperature (°C)</td>
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<tr>
<td>Support mode</td>
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3. MRI experiments

3.1 Subtraction image acquisition test

An MRI imaging experiment is carried out while a laboratory rat is fixed to the head positioner created by the 3D printer. Figure 8 shows a setting situation of a rat for an MRI experiment. The MRI is a 1.5T-compact MRI (MRminiSA MRT-A1508AC, DS Pharma Biomedical Co.Ltd.) (Yamada, et.al., 2015). The rat fixed to the head positioner is installed to the solenoidal coil. A rubber heater is put to the rat to maintain the rat’s body temperature.

Figure 9 shows an example of the MRI experiment with using the conventional head positioner. This experiment is carried out to obtain a subtraction between before and after contrast medium administration in order to get clearer brain image. The contrast medium is a chemical substance, which is administrated into the rat, in order to enhance the contrast of body structures for MRI.

In the Fig.9, yellow line means a coronal image position shown in right image. This conventional head positioner often cause a rotation around the axis line of the bed curve as shown in the right part of Fig 9 (a), because this conventional head positioner cannot fix the rat properly. Also, the teeth of the rat often tear often loose from the incisor bar due to the rat’s body motion as shown in Fig.9 (b). As the result, the adequate subtraction image cannot be obtained as shown in Fig.9 (c).

The head positioner developed in this research never occurs this situation, because both the teeth and whole head of the rat is fixed properly. Figure 10 shows the subtraction image with using the developed head positioner. A clearer image of soft tissue can be obtained with eliminating other parts. This result is achieved by satisfying the required specification 4.

Figure 8 Setting situation of a rat for an MRI experiment
(a) MR image before contrast medium administration with using the conventional head positioner

(b) MR image after contrast medium administration with using the conventional head positioner
(Teeth of the rat often tear loose from the incisor bar due to the rat’s body motion)

(c) Subtraction image between (a) and (b) images
Figure 9 MRI experiment with using the conventional head positioner

Figure 10 Subtraction image with using the developed head positioner
3.2 Fixing performance test

Figure 11 (a) and (b) show $T_1$-weighted and $T_2$-weighted coronal images of the rat’s head, respectively. $T_1$-weighted and $T_2$-weighted images are often used in medical fields to analyze the tumor position and so on (Damadian, R., 1971). In brief, water is treated as low signal to generate all images for $T_1$-weighted images and is treated as high signal to generate all images for $T_2$-weighted images, respectively. These images enable to identify anatomic locations or analyze the tumor.

Clear coronal section images can be obtained as shown in the figures with comparison of the ones with using the conventional head positioner shown in Fig.9 (a). There are no bulk motion, because the breathing and other motions are reduced greatly due to the developed head positioner. The head is installed in the detected range of the solenoidal coil properly and high SNR (Signal Noise Ratio) (Miyagi, 2010) can be obtained in wide area.

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Figure 12 (a) and (b) show sagittal image of the rat’s head with using the conventional and the new head positioners, respectively. As shown in figures, top head become flat with using the new head positioner. That is to say the rat’s brain is taken with the same angle of the Atlas. This result is achieved by satisfying the required specifications 1 and 4.

When olfactory bulb or cerebellum of the rat must be analyzed, the position can be adjusted by sliding the bed as show in Fig.13. Yellow lines in upper images correspond to a detection point of MRI and lower images correspond to coronal images at the detection point of MRI. This head positioner have versatility for various experiments. In fact, this head positioner is began to be used in a collaborative research institute. This head positioner will be a fundamental device to support many basic medical researches.

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4. Conclusions

A novel design of rat's head positioner for MRI was newly proposed and its feasibility was demonstrated. The design of the head positioner had not been discussed in detail from the viewpoints of mechanical engineering so far, this was an important and a unique approach to support the basic medical researches.

The obtained results are the followings.
1. A process flow from CT data of the rat to a creation of the rat's head positioner was established.
2. Several specifications required for a rat's head positioner were revealed by some preliminary discussions and various preliminary experiments.
3. A novel design to fix a rat was proposed with satisfying the required specifications.
4. A feasibility of the proposed head positioner was demonstrated through an MRI experiments.

Future work is that some amendments will be added to the head positioner, when some problems will be appeared through various MRI experiments.

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References