論文

Construction of a large scale 3D image database of human brain

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Nowadays, highly advanced medical imaging devices, like MRI(Magnetic Resonance Imaging), are developped and have become rather common apparatus for medical research of the human brain. No matter how much data is obtained, however, it is nothing without appropriate measure for searching and analyzing it. The necessity of sophisticated database management systems for three-dimensional brain images is now clear.

A three-dimensional brain image database which consists of about 1000 brain images taken from normal subjects are under construction. In this paper, what have accomplished on the database up to now will be introduced and several issues on general design of such kind of database are discussed.

1 Introduction

Development of various medical imaging devices enables us to obtain vast amount of three-dimensional data on the final frontier of modern science: the human brain[1]. The vastly accumulated data is, however, nothing without appropriate measure for searching and analyzing. The necessity of sophisticated database management systems for three-dimensional brain images is now clear.

The brain images, each of which is 4 to 16 megabytes large depending on format and resolution, should be easily selected and transfered via network and should be delivered to the desktop of the researcher dealing with brain image analysis. Once such a system is realized, the system will be utilized for constructing standard brains and clinical processes which are much helped by real-time searching of the brain images.

We have been constructing a three-dimensional brain image database which consists of about 1000 brain images taken from normal subjects. In the following sections, what we have accomplished on the database up to now will be introduced.

2 Requirement for the database

These point should be satisfied by such database systems.

2.1 Fast reaction speed

The large size of three-dimensional brain image is a challenging factor for present fast network systems. This situation is made worse by huge accumulation of data, because the necessity of mass-storage devices such as automatic tape/disk libraries are eminent. The robotics system which exchanges media give rise to further latency of data delivery and its complicated dependency on access pattern. Fast network itself, e.g. ATM or FDDI will exhibit several problems due to the large size of files to be transfered.

To study this issue, we have employed an ATM network which is spread among several medical institutes and is rather heterogeneous[2]. Also we have a CD-ROM based mass-storages device. We are trying to check how efficient the data distribution can be on this hardware and to improve it.

2.2 Extended data-usability

In these kind of database systems, the idea of data-usability should be far more extended than they are in the conventional databases. The theoretical background of the relational database management systems(RDBMS) is proven to be very useful to organize various kinds of complicated data structure. It seems, however, that the RDBMS does not offer much help in the case of image database. This is especially true when the organization of the images are flat and relationship between images are mainly defined on-the-fly manner, as in the case of ours.

Flexible image handling and easy access to the image processing tools gives far larger impact on data-usability. Also, since the database will deal with three dimensional images, which is hard to grasp for human user, the idea of data-usability should include accessibility to image visualization tools from the database. Otherwise, the users have to invoke image tools separately from database interface, hence the integrity of the whole system will be far degraded.

2.3 User-friendly interface

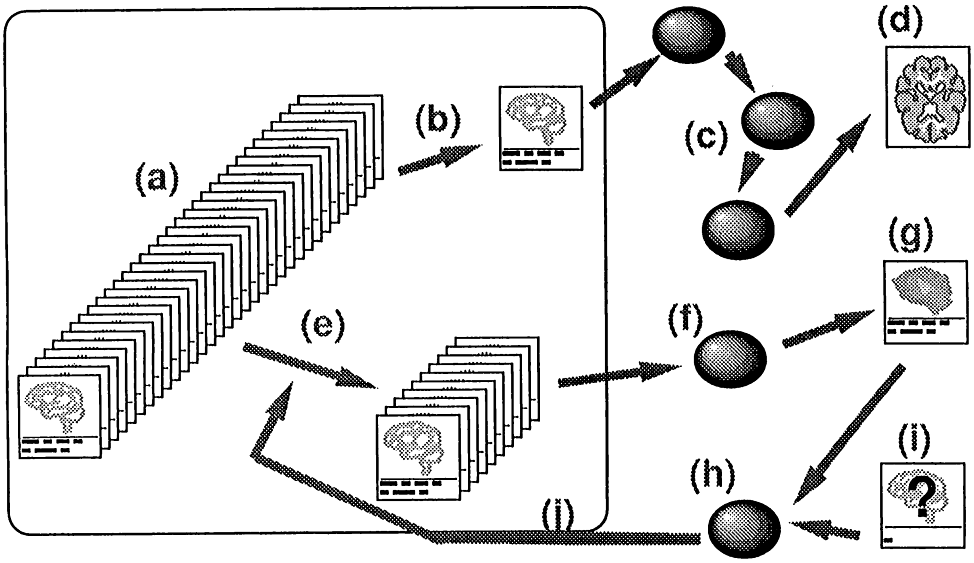
The system does not have to have so called "user-friendly" interfaces because all supposed users in this case are professional researchers or medical doctors. Nevertheless, detailed knowledge on the structures of the database should be hidden to users who are busy in their medical works. Nowadays, even the Structured Query Language(SQL)[3], which was originally designed for non-professional database users, is too complicated and assuming too much background on the structure of the database.

The World Wide Web(WWW)[4] guarantees an easy and graphical access from database to almost any kinds of client computers. And related technologies like the form interface and accompanied Common Gateway Interface(CGI) will be a nice alternative interface. The form interface is very intuitive and hiding details of the system well.

However, the form interface has a fundamental limit on the complexity of search conditions. Moreover, users of image databases tends to use complex search conditions in combination with various image processing procedures which might be under development and undergo daily changes.

In Figure 1, such a situation is exemplified. In the figure, the large rectangle at left of the figure represents the database system. Small rectangles are original and processed brain images. And elliptic objects are representing various image processing tools. A series of image processing should be applied to obtain typical representation of a image from the database ((a) in the figure) like a slice-view ((b),(c),(d) in the figure). As shown in the following section, the standard brains are calculated from certain group of images((e),(f),(in the figure). Such procedure might be repeated with different parameters as a kind of optimization process, ((h),(i),(j) in the figure) as discussed in the following section.

In these examples, the image data handling, the image processing and the handling of their result are so intertwined and kind of algorithm should be involved to perform the whole process. Character based interface like some kind of shell or command-interpreter will be more appropriate in such cases. Also, a script language function may be provided by such shell, which might be nice medium on which many other tools communicate each other. This will give rise to the above-mentioned



integrity of the image processing system.

3 The standard brains

We are especially interested in processing these brain images from normal subjects because the brain images without any lesion or defect must keep their natural forms. From natural forms, we can derive an average shape of the brain. Such an average is referred to as a standard brain. A standard brain is very useful for computational analysis of brain images because it gives us an anatomical mapping on the brain.

Also, such an average shape of brain might be useful for clinical application. If there is some statistically significant difference exists between a patient's brain and the standard with all condition (age, sex, etc.) the same as the patient, it might be understood as a sign of diseases.

In other words, by gathering normal brains, standard brains are able to be defined for each sub-set of the brain images. Image subsets consist of brain images from subjects who have any special attribute such as male, female, special metabolic problems, in common. Then we can discuss several issues by means of the standard brains.

Firstly, when a new brain with known attributes is given, the standard brain of the sub-set with the same attributes can be used as template of pattern recognition to identify each part of the brain. Such process is called registration in the field of medicine. The parts of the brain to be identified are, namely, the frontal lobe, temporal lobe, occipital lobe, and parietal lobe. These are corresponding to front, side, top, and dorsal parts of the brain, respectively. And more detailed registration can be done in similar manner. Using finer subset, that is, specifying more conditions for sub-sets which standard brain based on, is effective to improve precision of the registration. Today, automated registration is highly advanced[5], but it still is imperfect and often needs human supervision or final check on the result. Hence, the result, in a form of color-coded image, should be related to and organized with the original image in the database.

Secondly, when a newly given brain's attributes are unknown, the difference from the standard brain will be helpful to decide whether it should be included to the sub-set. This will be helpful for clinical diagnoses by taking the standard brain of the healthy subset. Specifying more conditions give rise to reliability of diagnosis. For example, the reduction of brain volume, which is not rare in elderly people, may be diagnosed abnormal taking a standard brain of whole population as the benchmark. This can be avoided by using a standard brain defined for people elder but proven as healthy. In such a task, brain images which satisfy certain conditions should be handled as a group, so that reseacher's workload is minimized.

Thirdly, when standard brains are defined for more than one sub-sets on which we expect some meaningful difference, comparing the standard brains of those sub-sets are best way to evaluate the difference of the sub-sets. Also, for sub-sets parametrically classified, such a procedure is useful for parametric understanding of the difference. This is especially interesting when the parameter is the age, because this is verily clarifying the mode of aging of the brain, which is very important theme of medicine in the near future. However, to discuss effects of various factors on retarding or aggravating the aging, the standard brain should be made for various subsets on demand. In this case, if calculating a standard brain for particular subset can be initiated by single command, it is the ideal way of introducing abstraction to database. Again organization of images and image processing tools is important.

4 Source of the brain images

As explained above, the normality of the subjects is especially important. All brain images should be free from defects. All brain images incorporated into the database should be taken from subjects who are free from diseases which can affect the shape of the brain. At the same time, the number of the subject is also important for reducing the statistical error of the standard brain. As subjects, we have been inviting volunteers.

Having noticed that considerable number of the volunteers who claim to be healthy by themselves have severe diseases, we are carrying out the following screening procedure for every one of the volunteers.

After the agreement to conditions of our research project and confirmation of ones "informed consent", every one of volunteers is examined by a doctor of our team, and a set of MRI images of ones brain is taken. The data obtained from examination process is recorded in a form of questionnaire. This data will be introduced later as attribute data of the brain images. The doctors of our team check the state of the subjects by means of the MRI images and classify them into following five classes.

A. No lesion is recognized in their brain images.

B. Limited number of lesion are recognized.

C. Worse than B. However, practically they are health.

D. Severe problem is found in their brain. These subjects are introduced to clinical doctors. Since all our procedure is just for quick screening of unhealthy brains, further formal examination is recommended for subjects classified to this class. They are not included in our data base.

O. The brains in this group are actually belong to one of A, B, and C, class. However, some problem is found in the MRI images, somewhere but in the brain. Namely, they have problems in their ears or nose. These subjects are introduced to the otorhinolaryngologists.

X. There is a problem on quality of the MRI images. Possibly a mistake in the scanning. Occasionally, foreign objects, especially metal crowns of dentist on their tooth cause this kind of problem by its large magneto-susceptance. If such foreign objects can not be removed easily, the subject is simply released.

The brain images classified to A, B, and C, class will be incorporated to the data base.

5 Organization of the database

The brain images are stored into the database with their attribute data. The images are addressed and searched by using these data as keys.

Searching for images taking an image as a key, that is, automatic filtering of images based on similarity between the images and given key, is recently getting large attention. However, in our project, such kind of image searching is kept as a theme for future extension. Because image key is useful only if there are several subsets of images which are unlike to each other. Since all images in our database are normal brains hence the difference between them should be small.

The data model so far we have been using is a relational one. Its main key is the identifiers or the handles of the images related to various attribute data stored in the single table. There are other tables in the system (e.g. for user administration), in this paper they are not introduced for simplicity.

The following are the name of each field of data and its explanation. Some of them are directly corresponding to single SQL field. Others are corresponding to multiple SQL fields. These correspondence rules are also introduced. The datatype (float, character etc.) is decided to maximize the data usability of the completed system.

Some of the fields are directly related to particular diseases. We have selected these diseases according to our special interest on them and a natural assumption that only limited diseases have significant effects on shape of the brains.

5.1 Generic data

Subject ID: Consists of unique number and name of the institution the subject is accepted. The latter part is necessary because we are planning to gather MRI images from more than one institutes.

Age: An integer.

Sex: A string field contains either of "Male" or "Female".

Height: A floating number in centimeter.

Weight: A floating number in kilogram.

Blood pressure: Two floating numbers called BP_L and BP_H. They are translated from widely used notation like "80/170". The unit used for BP_L and BP_H is "mmHg".

Handedness: A floating number between -1.0 and 1.0. This value is the likelihood of the subject's handedness: -1.0 means completely left-handed. 1.0 means completely right-handed. This value is evaluated by a standard test[6].

MRI diagnose: The diagnosis made by doctor by means of the checking in advance which is described in chapter 4.

5.2 Life style

Smoking: Whether the subject ever have a smoking habit. Either Y or N.

Drinking: Whether the subject ever have a drinking habit. Either Y or N.

Smoking index: A floating number which describes how much is the subject currently smoking.

Drinking index: A floating number which describes how much is the subject currently drinking.

Profession: Current profession of the subject. A string field.

Exercise: What kind of exercise the subject is currently doing. A string field.

Hobby: What kind of hobby the subject is currently doing. A string field.

5.3 Psychological test

PSYCOTEST: Either Y or N, meaning whether the subject has cooperated in the psychological test. This field is necessary because the subjects are allowed to deny this part of examination if they do not want.

PSYCOVAL: Twenty-five floating values each of which are representing specific trend of the subject's psychology. Originally extracted from a standard test[7].

5.4 Current Diseases

For each of selected diseases, there are three fields describing whether the subject has the disease (Either Y or N), how long they have been with that (A floating number in years.), and what kind of meditation or treatment they have undergone (a string field). Selected diseases are:

- Hypertension
- Hyperlipoidemia
- Hypercholesterolemia,
- Diabetes

5.5 Past Diseases

Any diseases the subject have experienced, then recovered. A string field.

5.6 Past Diseases on Family

For each of selected diseases, there are five fields (Either Y or N) each of which represents whether the subject's parents, sibling, grandparents, children, and grandchildren have or had the diseases. Selected diseases are:

- Hypertension
- Hyperlipoidemia
- Hypercholesterolemia
- Diabetes
- Cerebral infarction
- Cerebral hemorrhage
- Subarachnoidal hemorrhage
- Psychiatric disorders
- Arrhythmia

5.7 Subjective symptoms

Headarch: Whether the subject is complaining headarch. (Either Y or N)

Vertigo/Dizziness: Whether the subject is complaining vertigo or dizziness. (Either Y or N)

Insomnia: Whether the subject is complaining problems on sleeping. (Either Y or N)

Ear ringing: Whether the subject is complaining a ringing in ears. (Either Y or N)

Forgetfulness: Whether the subject is complaining forgetfulness. (Either Y or N)

Auxiliary: Any complaint the subject makes. (A string field.)

5.8 Current usage of drugs

For each of selected kinds of drugs, there are three fields describing whether the subject has been taking the kind of drug (Either Y or N), how frequently they are taking that (A floating number in times per week.), how long they are taking the kind of drug on continuous basis (A floating number in years.). Selected kind of drugs are:

- Sleeping drugs
- Drugs for headarch / painkillers

Table 1. Subject statistics

	Male	Female
10-19	24	5
20-29	74	38
30-39	35	25
40-49	58	57
50-59	85	103
60-69	43	33
70-100	11	8

- Traditional Chinese medicine
- tranquilizers

Table 2. Time for completing operations

	Downloading	Invoking image software
Searching	4.0 Sec.	4.0 Sec.
Media Switching	4.0 Sec.	4.0 Sec.
Transferring	33 Sec. (12 Sec.*)	
Starting software		4.0 Sec.
Sum.	37-41 Sec. (16-20 Sec.*)	8-12 Sec. 8-12 Sec.

*: data compression by "gzip -9".

6 Current status of the database

Up to now, we have successfully gathered over 600 acceptably healthy brains among all age group of Japanese, and construction of the average brain is in progress.

The age/sex distribution shown in Table 1 is a little bit unbalanced. We are now trying hard to fix the balance so that the statistical error of standard brain is minimized.

We have simulated the situation which the full-scale database will face to, and checked the reaction time of search and image retrieval in the case of ATM-connection. The data file is 256 × 256 × 124 voxels large and each voxel has 16-bits (16252968 bytes). A typical search condition for single image retrieval was entered to the web-based interface from a ATM-connected client machine to simulate a user's action. The wallclock-time consumed for completing the downloading is measured and shown in the left hand side of Table 2. We also measured the reaction time for single media exchange by our robotics device and included it in the left hand side of Table 2, which gives the worst case reaction time for single image retrieval on the system. We can conclude the performance is enough for real-time image handling on ATM-connected clients especially with compression of the data files. However, access to multiple images will cause another negative impact on the performance via switching of medium. We have deviced a novel way to alleviate these problem [8] and introduced a simulation result of performance improvement.

As the first step of database construction, we have extracted about 100 brain images out of 600, and constructed a prototype database environment with minimum functions on a UNIX database server (DEC Station 4100 with 4CPUs) and a IBM-compatible type personal computer.

Following the above mentioned requirements for the interfaces, we have been developing two different prototypes each addresses different aspects of the requirement for interface. The web-based interface (Figure 2) provides the basic level accessibility and usability to the database[9]. It is connected to a prototype database as the backend. The backend is based on the Informix IUS 9.12 RDBMS working on a IBM-compatible type personal computer as well as the web-browser working as the interface. The search condition can be given to any combination of the database fields in the table-like interface. The web interface can deal with logical combinations of the search criterion by and/or selector in the rightmost column of the table. Once some of the images are selected, the user can specify local directory into which the selected images will be downloaded in a download dialog. Later, user may invoke any processing tools on the client machine.

The other interface we are developing is a character-based one. Actually, it is a programming environment on which users can execute a kind of script languages, currently an extension of the Perl5 [10]. Because this is a kind of rapid-prototype, the key issue is the simplicity. Hence, the backend database is implemented on Perl5 as well as the interface. The database tables are stored into hash valuables of the Perl5. And, some of the functions like user administration and security issues are largely exploiting the UNIX environment's native functions. The system is implemented on the DEC Station server, which turns out to be fast enough to cover the efficiency problem of the interpreter language.

The main characteristics of the environment are,

- In general, object-oriented design is employed. By this, a modular design is enabled, and future extension will be easier.
- A search function by which users can filter the images by any condition on attributes of the images. This also provides full-text search on contents of string type attribute fields.
- Result of the search function can be substituted in Perl valuables. This enables utilizing the result for adjusting the condition of the next search. Moreover, it is very convenient to address a group of images by the name of single Perl array.
- A help function using full-text search on a repository. By this function, character-based interface can be even more user-friendly than web-based one.
- An extended history function, which can keep track of any file generated in the process of image handling and analyzing,. is under development. The efficiency of development of image processing on trial and error basis will be improved because the trace of such a task is automatically recorded.
- Since the environment is based on the Perl5, various tasks on the database can be executed by simple scripts which are directly executed by the Perl5.
- Image processing tools can be invoked directly from the environment. This gives rise to further integrity of the databa: image processing systems.

On such an interface, the user can implement rather complicated statistical operations. For example, an algorithm of cluster analysis of brain images may be implemented as a script in combination with the image processing tools, which can evaluate the similarity of brain images given by the database.

The reaction time of this interface is also measured and presented in the right hand side of the Table 2. In this case, retrieved image is not stored into the harddisk of the client machine, but is directly loaded by the image processing program to be presented in the display of the client machine. It is impressive that reaction time is largely improved by this way of handling images.

7 Conclusion

Toward the future research of human brains, construction of a large scale brain image databas is on its way. To clarify problems of the project, a prototype database was constructed and its basic performance was measured. Also, several issues on preferable interface of such kind of database is discussed.

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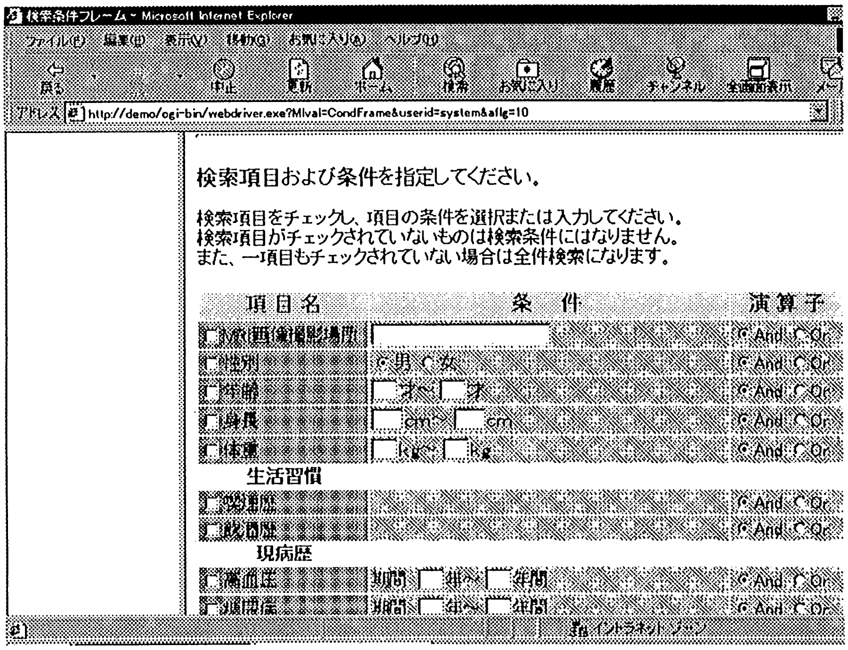

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