

**TIME-SENSITIVE COMMUNICATION OF DIGITAL
IMAGES, WITH APPLICATIONS IN TELEPATHOLOGY**

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TIME-SENSITIVE COMMUNICATION OF DIGITAL IMAGES, WITH APPLICATIONS IN TELEPATHOLOGY

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To my parents ...

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SUMMARY

Telepathology involves the practice of pathology at a distance, using enabling technologies such as digital image acquisition and storage, telecommunications services and infrastructure etc. In this thesis we address the two main technology challenges in implementing telepathology, viz. compression and transmission of digital pathology images.

One of the barriers to telepathology is the availability and the affordability of high bandwidth communication resources. High bandwidth telecommunication links are required because of the large size of the uncompressed digital pathology images. For efficient utilization of available bandwidth, these images need to be compressed. However aggressive image compression may introduce objectionable artifacts and result in an inaccurate diagnosis. The alternative of using zero compression or mathematically lossless compression is not feasible because of the excessive amount of information that would need to be transmitted over the limited network resource. This discussion helps us to identify two main design challenges in implementing telepathology,

1. **Compression:** There is a need to develop or select an appropriate image compression algorithm and an image quality criterion to ensure maximum possible image compression, while ensuring that diagnostic accuracy is not compromised.
2. **Transmission:** There is a need to develop or select a *smart* image transmission scheme which can facilitate the transmission of the compressed image to the remote pathologist without violating the specified bandwidth and delay constraints.

We addressed the image compression problem by conducting subjective tests to determine the maximum compression that can be tolerated before the pathology

images lose their diagnostic value. We concluded that the *diagnostically lossless* compression ratio is at least around 5 to 10 times higher than the mathematically lossless compression ratio, which is only about 2:1. We also set up subjective tests to compare the performance of the JPEG and the JPEG 2000 compression algorithms which are commonly used for compression of medical images. We concluded that JPEG 2000 outperforms JPEG at lower bitrates (bits/pixel or bpp), but both the algorithms perform equally well at higher bitrates.

We also addressed the issue of image transmission for telepathology by proposing a *two-stage transmission scheme*, where coarse image information compressed at diagnostically lossless (or lower) level is sent to the clients at the first stage, and the Region of Interest (ROI) is transmitted at mathematically lossless compression levels at the second stage, thereby reducing the total image transmission delay.

The rest of the thesis provides a detailed explanation of the challenges identified above and the solutions we proposed to counter these challenges to facilitate the implementation of an effective telepathology system.

CHAPTER I

INTRODUCTION TO TELEPATHOLOGY

Telepathology is defined as the practice of pathology at a distance using video imaging and telecommunications [55]. In telepathology, the diagnosis is made by viewing digital images displayed on a screen rather than viewing glass slides under a light microscope. According to the Armed Forces Institute of Pathology (AFIP) definition [2], it is the practice of pathology (consultation, education and research) using telecommunications to transmit data and images between two or more sites remotely located from each other. This allows a pathologist practicing in a geographically distant site to consult another pathologist for a second opinion, or to consult other pathologists who are experts on particular disease processes.

Telepathology can be considered to be a sub-specialty of the broader field of telemedicine. Telemedicine involves the transfer of electronic medical data (i.e. high resolution images, sounds, live video and patient records) from one location to another, using telephone lines, optical fibers, satellite links etc. Besides diagnostic pathology telemedicine is also common in other medical specialties such as dermatology, oncology, radiology, surgery etc. It is mentioned in [6] that the practice of telemedicine has been around since the 1960's, pioneered by the National Aeronautics and Space Administration (NASA) and also lists other significant milestones marking the progress of this field of telemedicine. Due to the wider use and ease of availability of digital radiology images, teleradiology has been around for a relatively long time as compared to telepathology. In fact, the term "telepathology" was first used only recently by Weinstein [53] in a 1986 editorial written for Human Pathology. In this article he proposed the integration of robotic microscope, imaging technology,

and broad-band telecommunication for wide-area pathology networks. Since then the field of telepathology has made considerable progress with numerous articles, journal issues and conferences dedicated to the discussion of telepathology. In this chapter we briefly discuss the different telepathology systems (§1.1), the various applications of telepathology (§1.2) and the challenges in implementing telepathology (§1.3).

1.1 Telepathology systems

All telepathology systems can be broadly classified into two categories: static telepathology involving transmission of still images, and dynamic telepathology involving transmission of live video data.

1.1.1 Static telepathology

Static telepathology [54] is the simplest form of telepathology. Static telepathology, also known as *passive telepathology* can be defined as the practice of pathology at a distance based on the transmission of still or stationary images from pathology specimens for their interpretation and diagnosis. Static telepathology operates in a store and forward manner, where the digital image is captured at one end and then transmitted to the remote pathologist. The most basic form of static telepathology involves the capture of static images by a digital camera which is attached to a microscope and the distribution of this image to the remote center via e-mail [32]. Static telepathology is popular because it has low equipment costs (since robotic microscopy is not used) and low telecommunication costs (since image data is considerably smaller than video data).

The disadvantage of static telepathology is that the consulting pathologist at a remote location has little or no control over the microscope and has to rely on the referring pathologist to select the tissue fields. If the transmitting operator selects inappropriate histological fields, there might be a discordance between the evaluations performed using static image analysis and conventional microscopy [52]. Since the

referring pathologist is responsible for image sampling it is essential that the referring pathologist is a competent professional pathologist with basic knowledge in pathology informatics.

1.1.2 Dynamic telepathology

In dynamic telepathology, also known as *active telepathology* the images are captured and transmitted in real-time and the remote pathologist has a complete control over which part of the slide he or she is browsing [11]. In its most complete form the microscope is fitted with a robotic control for stage movement, focusing and objective lens selection so that distant operators have complete control over the images which they are viewing. The biggest advantage of dynamic telepathology is that it is almost identical to using a conventional light microscope, with no reliance on the referring pathologist for field selection. The disadvantage of dynamic telepathology is that the cost of the robotic setup and the high bandwidth links which are essential for facilitating real time communication is considerably higher as compared to static telepathology.

1.1.3 Hybrid telepathology

Static telepathology systems facilitate transmission of high resolution static images, but result in insufficient diagnostic accuracy due to the field selection problem. This problem can be avoided in dynamic telepathology by allowing transmission of real-time video but may require compensating on the spatial resolution of the video frames due to unavailability of sufficiently high-bandwidth communication links. Hybrid telepathology systems [60] combine the features of dynamic and static telepathology by allowing the acquisition and transmission of both dynamic real-time video and high resolution static image simultaneously at reasonable cost. For example, in the hybrid dynamic/store-and-forward telepathology system used in [15], the resolution in the dynamic mode was $350 * 288 * 24$ -bit color and the spatial resolution of the

static images was $1520 * 1144 * 24$ -bit color. By allowing consulting pathologists to alternate between static and dynamic mode as and when required, the amount of time used for controlling the robotic microscope is reduced and the benefit of high resolution static images is preserved while limiting the selection bias phenomenon.

1.1.4 Virtual Microscopy

Virtual microscopy [45] is another emerging technology for telepathology, where multiple digital images at different magnifications are acquired and integrated into a large virtual slide which is stored on a server for remote inspection by the client. It is implemented as a software system employing client/server architecture and attempts to provide a realistic emulation of a high power light microscope. A virtual microscope implementation is expected to allow the following functionality ([16]): a) fast browsing through the slide to locate an area of interest, b) local browsing to observe the region surrounding the current view, c) changing magnification, and d) changing the focal plane. To facilitate low-latency retrieval and browsing of large volumes of medical data, compression, transmission and placement or organization of the images on the remote server become the critical factors determining the design of the virtual microscopy system. The main advantage of virtual microscopy is that it emulates the behavior of the physical microscope and is much more cost effective compared to a dynamic telepathology setup.

Further classification of different telepathology systems into first, second and higher generation systems can be found in [55].

1.2 Applications of Telepathology

Telepathology can find the several applications as outlined in [56]. Some of these applications are discussed below,

1. **Remote primary diagnosis :** Using modern telepathology systems it is possible to view slides at a distance, operate a robotic microscope and make a

diagnosis by viewing digital images and videos on the computer monitor. In remote primary diagnosis telepathology, the diagnostic effort and responsibility resides entirely with the pathologist at the remote site.

2. **Second Opinion Pathology :** Using a telepathology system, a referring pathologist can easily request a second opinion from a specialist or consulting pathologist located at a remote facility. In second opinion telepathology, the diagnostic effort and responsibility resides with both the referring pathologist consulting pathologist. Telepathology can significantly improve the turn-around time by reducing the time spent in sending the glass slides or tissue blocks to the specialist by post. Moreover, if fast communication resources are available, interactive communication between the two geographically separated pathologists is also possible. [15] demonstrated that high concordance rates ranging from 99% to 100% were achieved for clinically significant telepathology and conventional light microscopy diagnoses of 2200 consecutive surgical pathology cases while using a hybrid dynamic/store-and-forward telepathology system. This and several other studies indicate that telepathology can be used to support an isolated pathologist for second or expert consultation or even to completely transfer the diagnostic work to a remote facility.

3. **Remote teaching :** A traditional microscopy classroom can be costly to set-up and to maintain, and high quality glass slides are impossible to duplicate or replace. Telepathology can offer a cheaper and more convenient alternative to conventional light microscopy for the purpose of education and training. As pointed out in [30], the important advantages of using virtual microscopy for education are that all users view the same image, and these images can be easily distributed using the Internet or other media. Further, virtual microscopy also enhances the instructor's ability to point out interesting features, and the

student's overall ability to learn from the slide.

Telepathology can be applied to all the forms of pathology [39],

1. In **Anatomic Pathology**, which involves the diagnosis of diseases by morphologically studying lesions introduced by diseases. E.g.: Frozen section diagnosis, biopsies, fine needle aspirations, cytology etc.
2. In **Clinical Pathology**, which is concerned with the diagnosis of disease based on laboratory analysis of bodily fluids such as blood, urine etc. E.g.: Applications in blood banks, cytogenetics, DNA analysis, hematology etc.

1.3 Telepathology Challenges

Several challenges [56] need to be overcome before a telepathology system can be employed for remote diagnosis and consultation. There are also potential legal problems in practicing telepathology as outlined in [13]. For example in the United States, doctors need licenses in each state in which they wish to practice medicine and hence its questionable if a pathologist can deliver his opinion to a patient located in a state where he is himself not licensed to practice. Further it is also uncertain if the liability lies with the remote pathologist, the reporting pathologist or a third-party providing the telepathology setup. There can be security and confidentiality concerns if the patient data is transmitted over a public network such as the Internet [3]. Also, concerns regarding the diagnostic accuracy of using digital images in place of physical slides need to be addressed [23, 51] before telepathology can be used in practice. Human factors such as aptitudes, abilities, attitudes and perceptions can also play a significant role in adopting telepathology in place of conventional microscopy [55]. There can be a considerable learning curve before the users acclimatize to the new technology and achieve viewing times (average viewing time per slide) in the same range as viewing times of pathologists using conventional microscopy [15]. It is also

possible that there is some psychological reluctance among practicing pathologists to this new field of technology.

Besides these legal and medical challenges, another barrier to implementation of telepathology is the availability and the cost of high bandwidth telecommunication infrastructure, network and services. High bandwidth communications links are required because of the huge size of digital pathology images which cannot be transmitted without compression. However there is a risk in using lossy compression for medical images in that, these lossy image compression algorithms can introduce artifacts which can result in an inaccurate; or in the worst case an incorrect diagnosis. The alternatives of using zero compression or mathematically lossless compression are not very feasible because they do not allow for adequate compression, which result in the transmission of excessive amount of information over the limited network resources. Clearly, compression and transmission of digital pathology images present significant challenges in the implementation of telepathology which we address in this thesis.

CHAPTER II

IMAGE COMPRESSION

Whole slide images (WSI) are extremely large. For example, a 20mm x 15mm region digitized with a resolution of 0.25 microns/pixel (mpp), using objective lens with 40x magnification, eyepiece with 10x magnification (total of 400x magnification) results in a image containing 80000x60000 or 4.8 Giga pixels (Gp). Typically this image would be represented as a color image using 24 bits/pixel (bpp) resulting in a huge file size of around 15GB. Further, if multiple focal planes (Z-planes) are used the resultant size can be in the order of several hundred gigabytes [12]. Clearly, storage and transmission of these images in uncompressed form is impractical; prompting the use of image compression algorithms.

Compressing raw images facilitates optimum consumption of valuable resources such as disk space and transmission bandwidth. Image compression is implemented by exploiting the inherent statistical redundancy existing in most of the images. Further compression is made possible by allowing some loss of fidelity. Compression schemes which allow losses in order to achieve higher compression are known as lossy compression schemes. Lossy image compression schemes work on the assumption that the entire image data need not be stored perfectly. Much information can be removed from the image data, and when decompressed the result would still be of acceptable quality. However, it is necessary to recognize that aggressive lossy compression can be potentially hazardous in case of medical images, since the artifacts introduced by lossy image compression algorithms can result in an inaccurate diagnosis. Hence the amount of information that can be removed or the compression level that can be achieved without reducing the diagnostic value of the image needs to be carefully

identified, as discussed further in this chapter.

2.1 Existing work

Since radiology is the dominant application domain for medical imaging technology, significant amount of literature is available on the topic of compression of digital radiology images. A review of the several lossless compression schemes such as Differential Pulse Code Modulation (DPCM), Hierarchical Interpolation (HINT), Difference Pyramids (DP) etc. and lossy compression schemes such as Vector Quantization (VQ) and algorithms based on the Discrete Cosine Transform (DCT) and the Discrete Wavelet Transform (DWT) etc. which may be used for digital radiology images is provided in [59] and [33]. [8, 17] investigate the utility of JPEG-LS and JPEG 2000 for compression of digital radiology images representing several different image modalities such as computed tomography (CT), Magnetic Resonance (MR), Ultrasound (US) etc. and conclude that both the compression schemes offer similar or better performance than JPEG and recommend their inclusion in the DICOM standard. [50] also compares the performance of the JPEG vs. the JPEG 2000 algorithm for digital mammograms in an attempt to provide more evidence to support adoption of JPEG 2000 for medical images.

[27] suggests the use of content based compression of images for static telepathology. Here, the authors propose using a ‘content based’ approach which combines visually lossless and lossy compression techniques by judiciously applying either in the appropriate context across an image so as to maintain diagnostically important information while still maximizing the possible compression. [31] studies the effect of image compression on telepathology and concludes that JPEG compression of images does not negatively affect the accuracy and confidence level of diagnosis. [36] proposes the use of the JPEG 2000 image compression algorithm for developing a virtual slide telepathology system by using some useful features such as scalability and

JPEG 2000 Interactive Protocol (JPIP) offered by the JPEG 2000 algorithm. Besides these few publications addressing the issue of image compression for telepathology or virtual microscopy, most of the published trials [11] verifying the diagnostic accuracy of telepathology have tacitly used the JPEG or the JPEG2000 algorithms for image compression, without an in-depth analysis of the diagnostic accuracy and communication efficiency.

The loss of information associated with the use of lossy image compression algorithms renders the use of such schemes controversial because of potential loss of diagnostic quality and consequential legal problems regarding liability. However significant compression can be achieved only by using lossy image compression schemes. To determine if the compressed image quality is ‘good enough’ for a particular application such as diagnosis, education, archival etc., three different approaches have been suggested in [10]. The authors compare the performance of the three measures: signal to noise ratio (SNR), subjective ratings and *diagnostic accuracy* for CT and MR chest scans compressed using vector quantization and conclude that there is a need to develop computable measures of image quality which take account of the medical nature of these images. Several other studies investigating the effect of image compression on digital radiology images can be found in literature. A similar study comparing two subjective measures: just noticeable difference (j.n.d) and largest tolerable difference (l.t.d) for maintaining diagnostic accuracy of digital pathology images can be found in [18]. The study indicates that remarkably high compression ratios can be tolerated in diagnostic telepathology. This understanding is taken into account and the concept of diagnostically lossless compression has been developed more recently in [57] as discussed in the next section.

2.2 Choice of compression level and compression algorithm

One aim of the proposed research is to achieve a good tradeoff between compression ratio and diagnostic accuracy. This requires choosing an appropriate compression level and a suitable image fidelity criterion which indicates the maximum compression that can be tolerated without introducing unwanted artifacts in the diagnostically important features of the image. In [57] the concept of diagnostic lossless compression was introduced. Here 8 images (formalin-fixed paraffin-embedded tissue sections) were acquired and compressed using JPEG at compression ratios varying from 15:1 to 122:1 and presented to a combination of surgical pathologists and pathology residents at Emory University. The results indicated that these images could be compressed using JPEG at compression ratios of the order 10:1 to 20:1 depending on the nature of the input image, without reducing the diagnostic accuracy of the images. Clearly this *diagnostically lossless* compression ratio is much higher than the compression ratio allowed for by a mathematically lossless compression scheme, which is only about 2:1.

One limitation of this study was that only JPEG - compressed images and uncompressed images were presented to the pathologists. However as mentioned before, the JPEG 2000 standard is increasingly being used for telepathology and virtual microscopy applications. Hence the proposed research aims to complement the results of [57] by setting up another subjective quality-analysis test to compare the performance of the JPEG and the JPEG 2000 image compression algorithms. Besides making recommendations for compressing pathology images, the proposed subjective experiment also attempts to compare the performance of the two compression algorithms for generalized non-medical images.

2.3 JPEG vs. JPEG 2000: A Subjective evaluation of image quality

Previous section described the efforts to establish the criteria of diagnostic losslessness to determine the maximum possible compression ratio that can be afforded without reducing the diagnostic value of the pathology images. The second part of the image compression problem was to develop or identify an algorithm suitable for compression of digital pathology images. This section describes the research carried out in conjunction with the work in [57] to evaluate the performance of the JPEG and the JPEG 2000 algorithms.

2.3.1 Image fidelity criteria and the need for subjective evaluation

The fidelity criteria employed to quantify the nature and extent of the information loss incurred due to lossy image compression can be broadly classified as objective fidelity criteria and subjective fidelity criteria [22]. For objective image fidelity metrics such as absolute error (AE), Mean Square Error (MSE) or Peak Signal to Noise Ratio (PSNR), the level of information loss can be expressed as a function of the original image and the decompressed output image. The subjective fidelity metrics evaluate the extent of information loss by using subjective evaluations of the distorted images by human observers. This can be achieved by showing the compressed images to a cross section of viewers, and then aggregating their evaluations in the form of averages, Mean Opinion Score (MOS) etc.

The main advantage of using the objective fidelity metrics is that they are simple to calculate. Also since they have a fixed mathematical representation, further operations based on using these metrics are simplified. For example an optimization problem requiring the determination of the optimum bitrate for a certain image compression algorithm such that the total distortion does not exceed a given minimum, is considerably simplified if the distortion is measured in terms of objective metrics

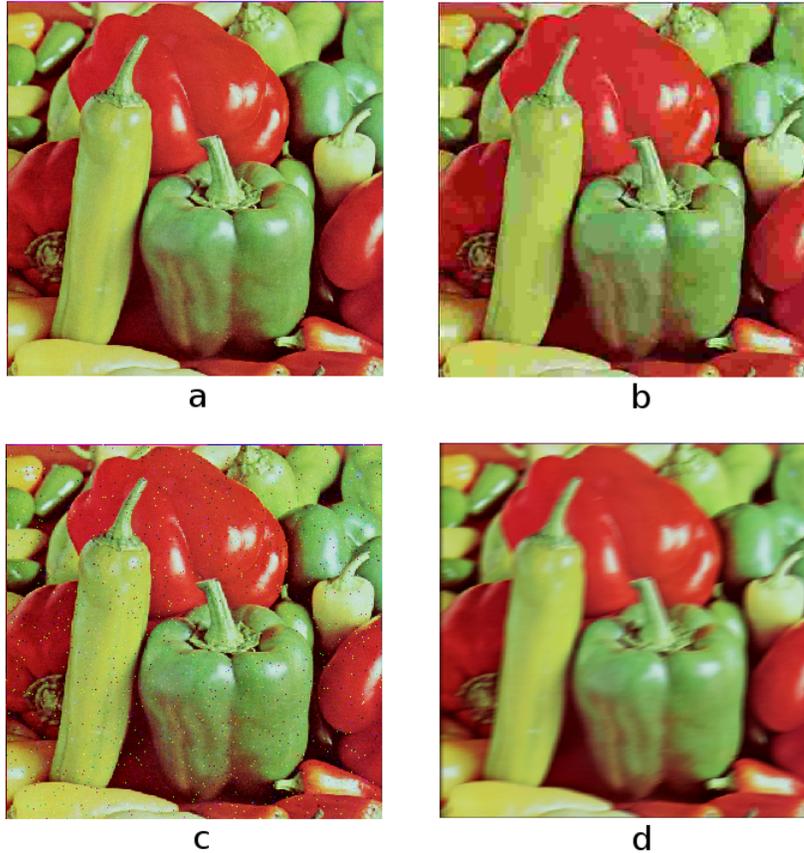


Figure 1: PSNR of images with different distortions but same **PSNR=24 dB**. a)Original Image, b)JPEG compressed image, c)Image corrupted by salt and pepper noise, d)Blurred Image.

having well-defined mathematical expressions. Unfortunately these simple objective metrics do not relate very well with the image quality. For example, Figure 1 shows that the original image suffers from distortion due to compression, noise and blurring. Each distorted image is perceptually different from every other image. However the PSNR for all these visually different images is 24 dB. This simple example shows that PSNR does not correlate well with the perceptual quality of an image and hence subjective evaluation is required to compare the visual quality of different images. The major disadvantage of subjective quality testing is that these evaluations can be very time consuming and may require additional resources depending on nature of the subjective test. In this chapter we discuss the design and results of a subjective

image quality analysis test which was conducted to evaluate the visual quality of images compressed using the JPEG and the JPEG 2000 image coding algorithms.

2.3.2 The JPEG and JPEG 2000 compression algorithms

JPEG 2000 and JPEG are ISO/ITU-T standards for still image coding. Both these standards support lossy compression and are widely used for natural images and sometimes even for medical images to achieve higher compression. In this section we will very briefly discuss the two standards.

2.3.2.1 JPEG

The JPEG standard introduced by the joint ISO/CCITT committee known as JPEG (Joint Photographic Experts Group) [26] is a very popular still image compression standard. The JPEG supports four modes of operation: sequential, progressive, lossless and hierarchical encoding [47]. Here, we will describe only the baseline sequential codec which implements Discrete Cosine Transform (DCT) based coding for lossy image compression.

Figure 2 illustrates the JPEG encoder/decoder when the 2D DCT/IDCT is used as the forward/reverse transform pair. In the baseline mode, the image (or individual color planes of a color image) are divided into 8x8 blocks and then each of these blocks are level shifted (to convert unsigned pixel values to signed integers) and transformed using the 2D-DCT. This results into 8x8 “DCT coefficients”, consisting of one DC coefficient and 63 AC coefficients. All coefficients are then uniformly quantized using a quantization table (can be pre-defined or user-defined). This quantization is the main source of loss in JPEG. After quantization the DC and the AC coefficients are processed separately. The DC coefficients are encoded as a difference between the current DC coefficient and the DC coefficient in the previous 8x8 block in the encoding order. Finally the coefficients are arranged in a zigzag sequence, and then entropy encoded using Huffman coding. The tables used for compression/decompression can

be pre-defined or generated by the particular application for a particular image using a statistics-gathering pass prior to compression.

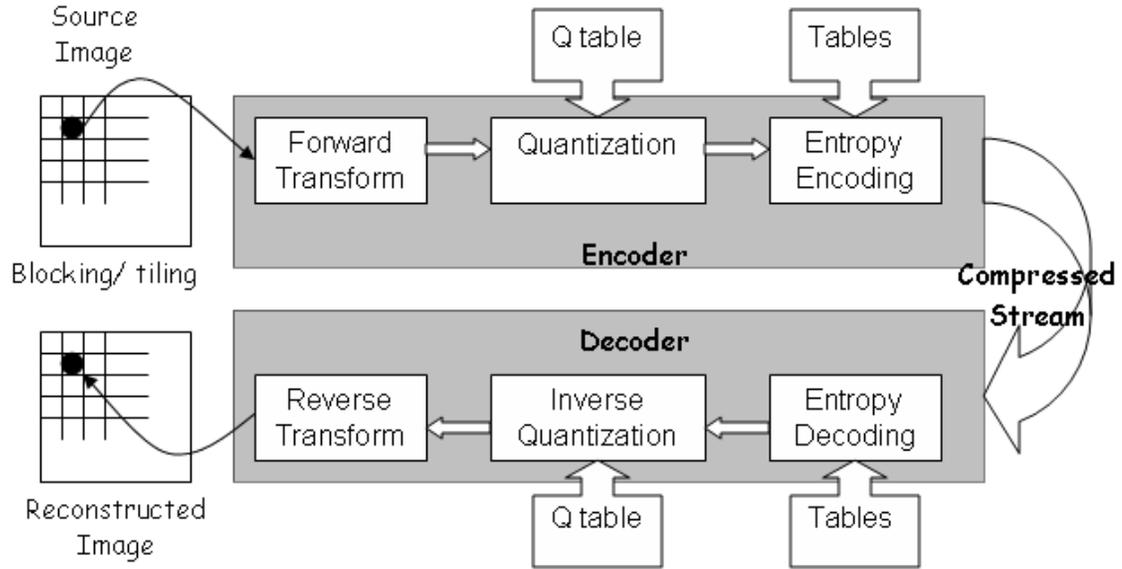


Figure 2: Block diagram of a transform based image encoder and decoder

2.3.2.2 JPEG2000

Several review articles such as [7, 38] and a comprehensive text [44] discuss the various aspects of JPEG 2000. The following description of the Part 1 of the JPEG 2000 standard is compiled from these three references. The JPEG 2000 standard is an outcome of the efforts undertaken by the JPEG committee to create a new image coding system for different types of still images (bi-level, gray-level, color, multi-component) with different characteristics (natural images, scientific, medical, remote sensing, text, rendered graphics, etc) allowing different imaging models (client server, real-time transmission, image library archival, limited buffer and bandwidth resources, etc) preferably within a unified system. The JPEG 2000 encoder /decoder resemble the one in Figure 2 where the 2D Discrete Wavelet Transform/Inverse Discrete Wavelet Transform (DWT/IDWT) is used as the forward/reverse transform pair. Before applying the forward transform, the source image is partitioned into

rectangular non-overlapping tiles of equal size. The tile size can be arbitrarily set and can be as large as the whole image. Further, each pixel value is level shifted (to reduce dynamic range and avoid complications such as numerical overflow during implementation) and then a reversible or irreversible color transform is applied to decorrelate the color data. The 2D DWT decomposition in JPEG 2000 is dyadic and can be performed using the reversible Le Gall (5,3) filter which allows both lossy and lossless compression and the non-reversible Daubechies (9,7) filter which allows lossy compression. The coefficients are then quantized using a central dead zone quantizer since it is R-D optimal for continuous signals with Laplacian distribution (such as DCT and DWT coefficients) and is independent for each sub-band.

The quantized wavelet coefficients are entropy encoded to create the compressed bit-stream. The entropy encoding in JPEG 2000 largely based on the embedded block coding with optimized truncation (EBCOT) algorithm, where each subband is partitioned into small rectangular blocks known as *codeblocks* (typically 64x64 size), and each codeblock is independently encoded. The independent encoding has many advantages such as random access to the image, improved cropping and rotational functionality, efficient rate control etc. The quantized wavelet coefficients are then encoded one bit at a time in a progressive manner; starting with MSB and proceeding to LSB. Each bitplane is encoded in three sub-bitplane passes: the significance propagation pass, the refinement pass, and the cleanup pass. For each pass, contexts are created which are provided to the arithmetic coder. The main advantage of this approach is that it allows a large number of potential truncation points (the bit-stream can be truncated at the end of each sub-bitplane pass), thus facilitating an optimal rate control strategy where the target bit-rate can be achieved by including only those passes in the output stream which minimize the total distortion due to compression.

In arithmetic encoding the entire sequence of source symbols is mapped into a

single codeword which is developed by recursive subdivision of the probability interval. In JPEG 2000, coding is done using context dependent binary arithmetic coding implemented by the MQ coder. In context-based arithmetic coding separate probability estimates are maintained for each context, which are updated every time a symbol is encoded in that context. With every binary decision, the current probability interval is subdivided into two sub-intervals, and the codestream is modified (if necessary) so that it points the lower probability sub-interval assigned to the symbol which occurred. The context models are always reinitialized at the beginning of each code-block and the arithmetic coder is always terminated at the end of each block.

2.3.3 Subjective Test Design

This section describes the design and the results of the subjective test. The aim of the test was to evaluate and compare images compressed using the JPEG and the JPEG 2000 algorithms.

2.3.4 Objective of the test :

The aim of this experiment was to study the merits of using the more recent JPEG 2000 algorithm over the popular JPEG algorithm for image compression. Two comparison criteria need to be considered here (see Figure 3),

1. **Comparison at a given bit rate :** It is of value to evaluate the visual quality of images compressed using the two algorithms, at the same bitrate or compression ratio. Thus this evaluation is carried out along the vertical lines seen in the Figure 3. The bpp along the x-axis is the free parameter in this experiment, and needs to be selected so as to cover the low - to- moderate ($\text{bpp} \leq 0.5$) and high ($\text{bpp} \geq 0.5$) bit rate ranges.
2. **Comparison at a given quality level :** It is also of interest to know at

what bit-rate is the quality of the JPEG compressed image comparable to the quality of the JPEG 2000 compressed image? The term quality can have various interpretations, for example it can be the quality factor (Q) specified by different JPEG codec/software or it can be the PSNR/MSE of the image. Thus with this experiment we wish to compare the compression performance of the two algorithms for a given value of Q or PSNR. So, in this case the evaluation is performed along the horizontal lines shown in the Figure 3 and the quality metric along the y-axis is the free parameter.

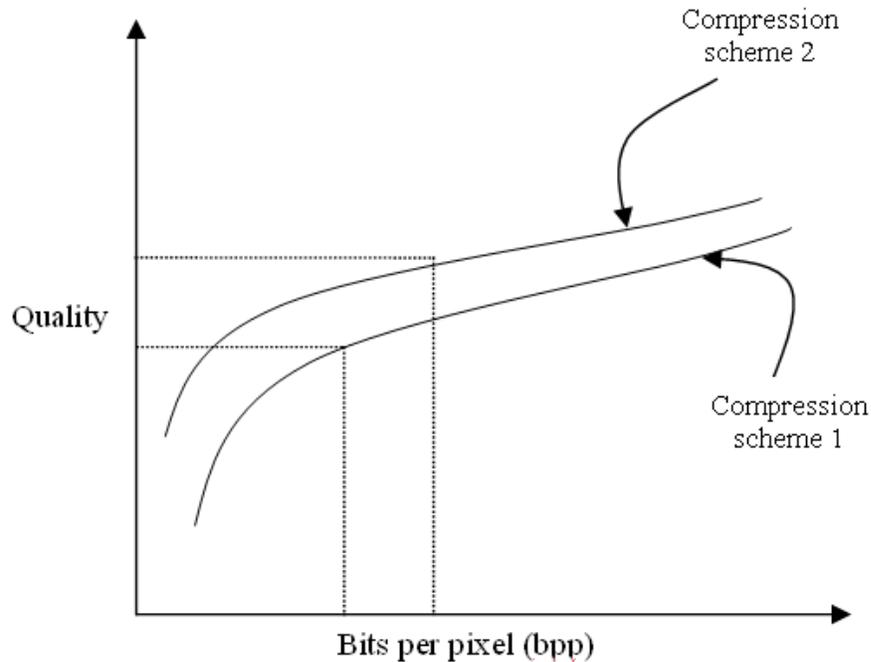


Figure 3: Illustrating the aims of the subjective experiment

2.3.5 Image database

Figure 4 and Figure 5 show some of the images used for this test. The images used in this experiment can be broadly classified into two categories: medical and non-medical images. The non-medical raw images used for this tests are obtained from the LIVE

database [40, 41, 49]. The medical images were obtained from Emory University and are a subset of the images used in [57]. The raw images then were then compressed using the JPEG and JPEG 2000 algorithms at bitrates ranging from 0.20 bpp to 1.0 bpp.

Typically, medical images are always compressed at higher bitrates because loss of detail due to aggressive compression can result in inaccurate diagnosis. Hence for this experiment, the medical images have been compressed at higher bitrates (bpp ≥ 0.5). The non-medical images could be compressed at lower bitrates depending on the application. Hence the non-medical images were compressed at bitrates ≤ 0.5 . Kakadu version 6.0 [28] was used for JPEG 2000 compression and the GIMP image manipulation software [20] was used for JPEG compression of the raw images.

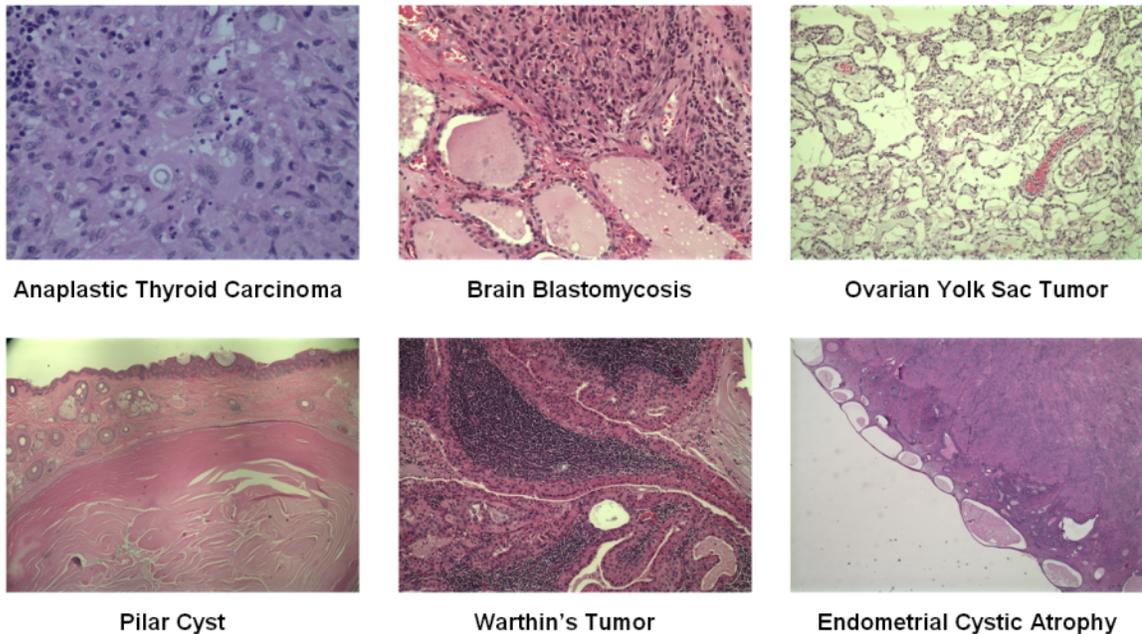


Figure 4: Collection of Medical Images used in Test2

2.3.6 Test Methodology

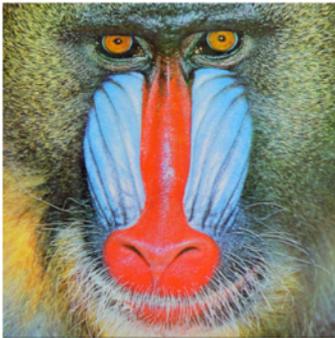
The subjective test was offered in the form of 3 tests: (*test1*, *test2* and *test3*). The subjects had the flexibility to complete all the three tests in a single session, or use



Buildings



Stream



Mandarin



Peppers



Barbara

Figure 5: Collection of Non-Medical Images used in Test1

multiple sessions to finish a single test.

1. **test1:** The aim of test1 was to compare the two compression schemes at lower bit-rates (0.2bpp - 0.5 bpp). The test consisted of 25 questions. For each question, the subject was presented with two images (*Image1* and *Image2*) displayed either side-by-side or placed one below another (if the image dimensions did not permit side-by-side display). One image was compressed using JPEG and another using JPEG 2000. The subject was then prompted to choose either *Image1* or *Image2*. For the case where the subject had no specific preference, two other options were provided: ‘*both*’ or ‘*none*’ implying both the images were satisfactory or neither image was of unsatisfactory quality. Additionally, the subjects were also invited to provide a free format qualitative comment.

The images chosen for this test were strictly non-medical. No specific ordering was followed while presenting the image pairs. Also, *Image1* or *Image2* were randomly associated with JPEG or JPEG 2000 schemes for each question to eliminate any obvious patterns in the display of questions.

2. **test2:** The aim here was to compare the two compression schemes at higher bit-rates (0.45-1.00 bpp). The test was presented in the same fashion as *test1*. Only the medical images were presented in this test. Thus *test1* and *test2* together covered a considerably wide range of bit-rates from 0.2 bpp to 1.00 bpp.

3. **test3:** This test was designed with the aim of comparing the two compression schemes for a given quality level. Here, six raw images (3 medical and 3 non-medical) were chosen and were compressed using JPEG 2000 at bit rates ranging from 0.25 bpp to 0.6 bpp. Also for each of these six raw image a set of four JPEG - compressed images were generated at bitrates residing within the range of (0, +0.15) bpp of the corresponding JPEG 2000 image. For example, if the JPEG 2000 image was compressed at a bit-rate 0.4 bpp, then the four JPEG images would have bitrates of 0.40, 0.45, 0.50 and 0.55 bpp. The questions were displayed in a randomized manner similar to the previous two tests.

A web-interface was specially designed for administering these tests. Figure 6 shows a screenshot when a question from Test2 is presented to the user. This simplified the process of distributing the tests since the subjects had the flexibility of completing the tests from their personal workstations. Guidelines specifying the recommended screen resolution and surrounding environment while taking the tests were

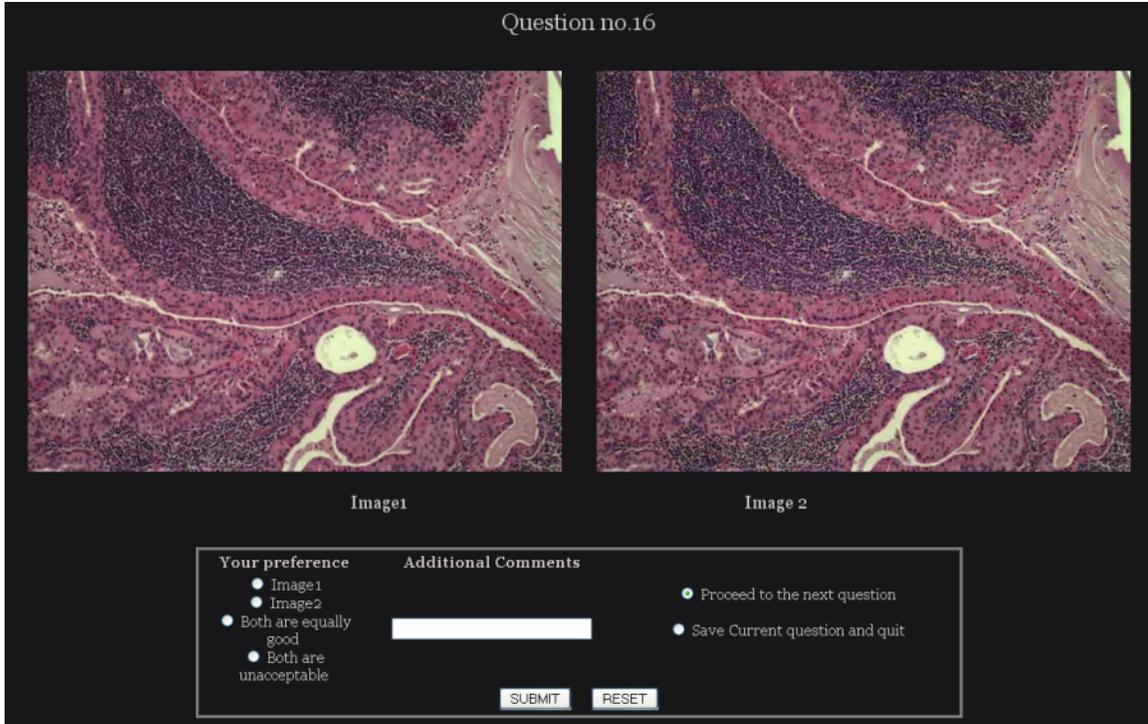


Figure 6: Screenshot showing how a question appears to the subjects

provided and the subjects were expected to follow these guidelines. Although the subjects were chosen randomly, eight out of the ten subjects who volunteered for the test claimed to be familiar with image compression standards.

2.4 Results and Discussion

For each question in *test1* and *test2*, the total number of users who choose JPEG or JPEG 2000 were counted and the compression scheme receiving more no. of hits was declared to be the winner. Table 1 shows that at low and moderate bit rates, i.e. between 0.2 bpp to 0.55 bpp JPEG 2000 is the clear winner. At higher bitrates (≥ 0.65) the difference in the visual quality between these compressed images seems to disappear and the subjects find both the images to be of acceptable quality.

Figure 7 and Figure 8 plots the Peak Signal to Noise Ratio (PSNR) for all the 10 test images compressed using JPEG and JPEG 2000 at bit-rates indicated on

Table 1: Test1 and Test2 results

Bitrate	Compression Ratio	Winner
0.20	120:1	jp2000
0.25	96:1	jp2000
0.35	68:1	jp2000
0.40	60:1	jp2000
0.45	53:1	jp2000
0.50	48:1	jp2000
0.55	43:1	jp2000
0.65	36:1	both
0.85	28:1	both
1.00	24:1	both

the X-axis. For a given bitrate, images compressed with JPEG 2000 have a higher PSNR than those compressed using JPEG. It can also be seen that in most cases the difference in the PSNRs of the two images reduces as the bit rate increases. The figures also show which compression scheme was declared as a winner for each of the test images, as indicated by the asterisk (*) on the PSNR curves. When the option ‘both’ was selected, the asterisk appears on the PSNR plots of both the compression schemes. It can be seen that there is no data point at which the image with lower PSNR is preferred over the image with higher PSNR. This shows that although the PSNR is not considered to be a good measure of the visual quality of an image, it is still somewhat consistent with the subjective results in that, they do not completely contradict the subjective preferences. However, we can also see that there is no correlation between the difference in the PSNR and the difference in the subjective quality of two images. As an example, for the *Barbara* and the *Pimen* image, the difference in the PSNR values of the JPEG and the JPEG 2000 images at 0.5 bpp is approximately the same (≈ 1.5 dB), but both images in the *Pimen* set are declared acceptable while only the JPEG 2000 image is declared as the winner in the *Barbara*

image sets. Similar scenario exists for the *Buildings* and *Mandr* images at 0.5 bpp. This implies that although the PSNR values do not completely contradict the results of the subjective evaluations, it is not possible to estimate the relative visual quality of compressed images from their PSNR values alone. Subjective experiments such as the one described here are necessary for this analysis.

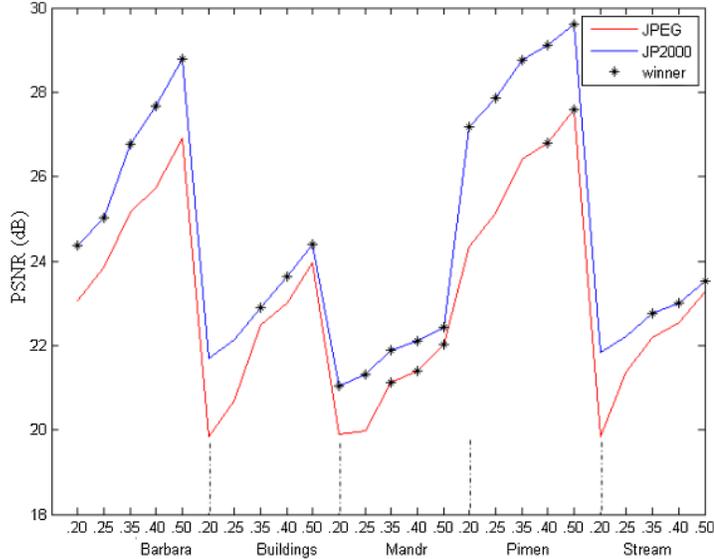


Figure 7: Results of test1

As mentioned in Section §2.3.3, some free-format qualitative comments were also collected from the subjects. Some comments made regarding the images compressed using the two algorithms are shown in Table 2. From the table we can see that the dominating artifact for JPEG 2000 was identified as *blurriness*, while that for JPEG was *blockiness*. It was also seen that almost on all instances where the subjects had a preference, the *blurry* JPEG 2000 image was preferred over the *blocky* JPEG image.

Table 3 shows the results for *test3*. These results compare the performance of the two algorithms, when both the compressed images are of the same quality. In this experiment we choose the PSNR to be a measure of the image quality. Thus the aim of this test was to inspect the compression ratio of the images which are

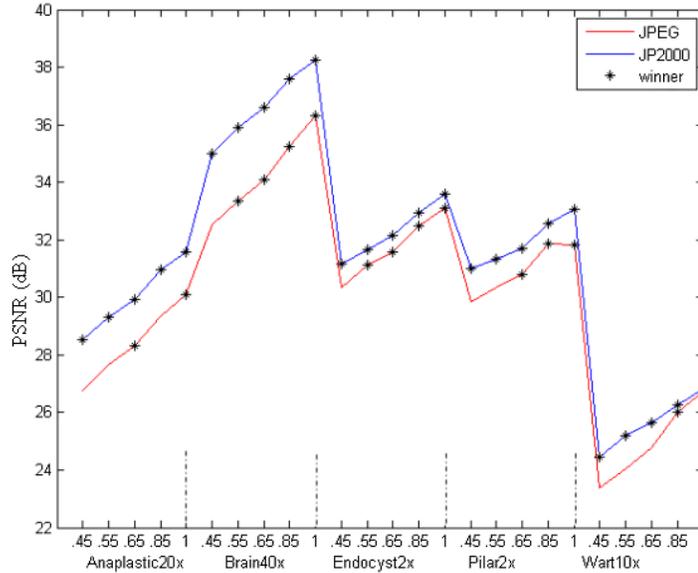


Figure 8: Results of test2

Table 2: Comments on the images presented in Test1 and Test2

JPEG	JPEG 2000
<i>blocky</i> <i>pixelated</i> <i>has funny edges</i>	<i>blurry</i> <i>fuzzy</i>

compressed using JPEG and JPEG 2000 in such manner that both the images being compared have approximately the same PSNR. The results indicate that for a JPEG compressed image to be visually equivalent to a JPEG 2000 compressed image, the former would need to be compressed at a bitrate which is at least 0.1 bpp higher than the later. For example, an image compressed using JPEG 2000 at a bit rate of 0.45 bpp looks visually equivalent to the same image compressed using JPEG at a bit rate of 0.55 bpp.

Table 3: Test3 results

Bitrate- JPEG2000	Bitrate- JPEG	Winner
0.25	0.25	jpeg2000
	0.30	jpeg2000
	0.35	jpeg2000
	0.40	jpeg
0.4	0.40	jpeg2000
	0.45	jpeg2000
	0.50	jpeg2000
	0.55	jpeg2000
0.45	0.45	jpeg2000
	0.50	jpeg2000
	0.55	jpeg2000, both
	0.60	jpeg2000, both
0.6	0.60	jpeg2000
	0.65	jpeg2000
	0.70	jpeg2000
	0.75	jpeg

2.5 Summary and Conclusions

1. The results tabulated in Table 1 indicate that at low and moderate bit rates (0.2 bpp to 0.55 bpp) JPEG 2000 is the clear winner. At higher bitrates (≥ 0.65) the both the compressed images appear to be visually equivalent.
2. Most users identified *blurriness* as the dominating artifact for images compressed using JPEG 2000, and *blockiness* compressed using the the JPEG algorithm as seen in Table 2.
3. From the results tabulated in Table 3, we also concluded that an image compressed using JPEG 2000 is visually equivalent to an image compressed using JPEG at a bitrate which is at least 0.1 bpp higher.

After analyzing the results of these subjective tests we can recommend using the

JPEG 2000 algorithm for low bitrate applications such as video surveillance. For medical imagery where the compression ratio is typically kept low, the two compression algorithms are visually equivalent and either the JPEG or the JPEG 2000 algorithm can be used. If computational complexity is not a constraint then the JPEG 2000 algorithm is preferred because it provides other important features such as scalability and region of interest coding. The work described in this section has provided a framework for using JPEG (and preferably JPEG2000) in future research with digital pathology images, with additional innovations described in the next section.

CHAPTER III

IMAGE TRANSMISSION

In the previous chapter we addressed the issue of identifying compression levels and compression algorithms suitable for transmission of digital pathology images. Although using lossy compression can significantly reduce the amount of information that needs to be communicated, these compressed images may still account for around 400 MB to 1 GB of data. This means that simply using lossy or diagnostically lossless compression cannot entirely solve the problem of transmitting the pathology images, especially when subject to stringent delay and bandwidth constraints. In this chapter we will attempt to develop a ‘smart’ image transmission scheme suitable for telepathology applications.

3.1 Existing work

Several articles have been published discussing the experience of individual organizations and institutes with telepathology. A review of these published trials show that a variety of telecommunication technologies such as Local Area Network (LAN), Wide Area Network (WAN), Integrated Services Digital Network (ISDN) and media such as telephone lines, coaxial cables, optical fibers etc. been employed for communication of pathology images. A comparison of three telepathology systems: ATM-TP (ATM based video conferencing system), TPS telepathology system (connection via LAN) and TELEMIC (Internet based control of a remote microscope) for primary frozen section diagnosis is done in [24]. More information regarding these telepathology solutions can be found in [24] and the references within. Two important requirements for frozen section diagnosis are good diagnostic accuracy (low rate of false positive/negative cases) and quick turn-around (short time for diagnosis). The

authors concluded that in terms of diagnostic accuracy and average diagnosis time per case, all the three solutions are well qualified for routine frozen section diagnosis. The authors have also extended to LAN based TPS system to use 2 ISDN lines thus facilitating intra and inter hospital telepathology. In [35] a long coaxial cable is used to implement an intra-hospital live telepathology system between the intraoperative consultation room and the pathology department.

In [46] an implementation of a dynamic telepathology system using the public telephone network is presented. The system is slow due to the use of low bandwidth telephone network, but is cheap and achieves a diagnostic accuracy of around 85%. The hybrid telepathology system [60] mentioned in §1.1.3 has also been configured for transmission over ISDN or T1. In [29] a telemedicine system is presented which uses ISDN, T1 and an optical fiber network to provide a wide variety of bandwidth options (from 28 Kbps to 155 Mbps) depending upon the nature of the telemedicine application. In [19] the feasibility and diagnostic accuracy of frozen-section confirmation/consultation using a telepathology system employing a ultra portable computer and wireless telecommunications in the form of Wireless LAN (IEEE 802.11 a/b/g) and Wireless WAN (EDGE and GPRS mobile technologies) is presented.

In [25] the authors make the strong case for using the Internet as an inexpensive communication resource for either static or dynamic telepathology and also provide several examples of existing systems using email, FTP, video conferencing etc. for telepathology. A telemicroscopy system consisting of a telemicroscopy server comprising of a computer with Internet access connected to the automatic microscope and the telemicroscopy client, who remotely operates the microscope is demonstrated in [37]. The authors claim that such simplified systems would allow any pathologist with Internet access to become a remote consultant without requiring access to any specialized hardware or software. The virtual microscopy systems mentioned in §1.1.4 also allow the remote clients to browse the huge whole slide images stored on the main

server using the Internet. Besides the few articles mentioned above, there are several other telepathology systems utilizing one of the possible options listed in Table 4 for image transmission. It seems that a particular telecommunication solution is chosen depending on the nature of the telepathology application, ease of access to high bandwidth networks and affordability of the entire telepathology setup including the image acquisition, archival and transmission hardware and software. For example a time sensitive application such as frozen section diagnosis has more demanding delay requirements and requires access to high bandwidth solutions provided by optical or ATM based networks, but results in increased overall cost.

Table 4: Bandwidth spectrum for telepathology

Technology	Theoretical line rates
POTS (Modem)	4.8 Kbps to 56 Kbps
ISDN	128 Kbps
T-carrier	1.544 Mbps to 400.352 Mbps
Etherent (Traditional, Fast, Gigabit)	10 Mbps to 1 Gbps
WLAN (IEEE 802.11 a/b/g/n)	11 Mbps to 300 Mbps
Optical links (SONET/SDH)	51 Mbps to 10Gbps and beyond

Although it is not possible to identify a single system that would work for all telepathology applications while keeping in consideration the different cost, bandwidth and other constraints it is quite obvious that irrespective of the technology used, transmission of the rich still images, real time videos or large virtual slides is not a trivial problem. Most of the solutions attempting to address the problem

of medical image transmission focus on trying to reduce the amount of information that needs to be transmitted by employing image compression schemes described in the previous chapter. Other approaches attempt to rearrange the image data into so-called *image pyramids* [21] or progressive structures [48] to allow user-friendly browsing of virtual slides stored on the remote server. Besides these, we did not find many solutions which attempt introduce any kind of ‘intelligence’ within the transmission mechanism itself, which would simplify the problem of image communication for telepathology. In this chapter we propose a *two-stage transmission scheme* to addresses the challenge of image transmission with considerations to diagnostic accuracy and time - sensitivity of telepathology applications.

3.2 Characterizing the value of two-stage transmission of rich images for telepathology

As mentioned in the previous section, transmission of digital pathology images becomes a very challenging task for time - sensitive applications such as frozen section diagnosis or real time dynamic telepathology. Delay targets can be very stringent also in the case of interactive applications such as virtual microscopy, which try to emulate the behavior of a conventional light microscope. For interactive applications the amount of wait time that can be tolerated by the users is quite small; sometimes as small 5-10 seconds. Due to insufficient bandwidth resources the demanding delay requirements cannot be met which prompts the need to develop a ‘smarter’ transmission scheme designed to address the time-sensitive nature of telepathology applications.

In this chapter we describe the proposed *two-stage transmission scheme*, where coarse image information is compressed at DL (or lower) level and sent to the client at the first stage. Once the Region of Interest (ROI) definition is received from the remote pathologist, the ROI details are transmitted at the ML level in the second stage. Figure 9 shows an example of image compressed using region of interest coding

feature offered by JPEG 2000 algorithm [4]. The annotated areas were identified by the pathologist as the features of interest (FOI) or ROI due to presence of *dark atypical nuclei with irregular bodies (circles) and vessels with palisading nuclei (freehand annotations)*. The region of interest appears to have a higher quality as compared to the background which appears blurry and discolored.

Further in this chapter, we develop a simple expression to determine the *bitrate budget* for a telepathology communication link subject to bandwidth constraints. Finally, by using the concept of two-stage transmission and the proposed bitrate budgeting mechanism we evaluate the value of employing the two-stage transmission scheme in place of a single stage transmission of the entire image.

3.2.1 The two-stage image transmission scheme

Ideally, medical images should be transmitted without any compression or by compressing the entire image at a mathematical lossless level. In order to reduce the amount of data to be communicated the images can be compressed at a diagnostically lossless level; thus giving a higher compression ratio of the order 10:1 to 20:1. However since DL level is a subjective image evaluation measure, if the entire image compressed at DL it may still contain some artifacts which are objectionable for some pathologists. To overcome this problem, the concept of region of interest can be utilized. In case of telepathology, the ROI can be defined as the diagnostically interesting areas within the pathology images, where absolutely no loss or compression artifacts can be tolerated. Thus the ROI definitely needs to be compressed at ML level. The rest of the image (called as background or BG) is not required for diagnosis and hence can be compressed at the DL level or lower. Thus using region of interest based compression helps us to achieve the desired rate-distortion tradeoff, or in this case the bitrate-diagnostic accuracy tradeoff.

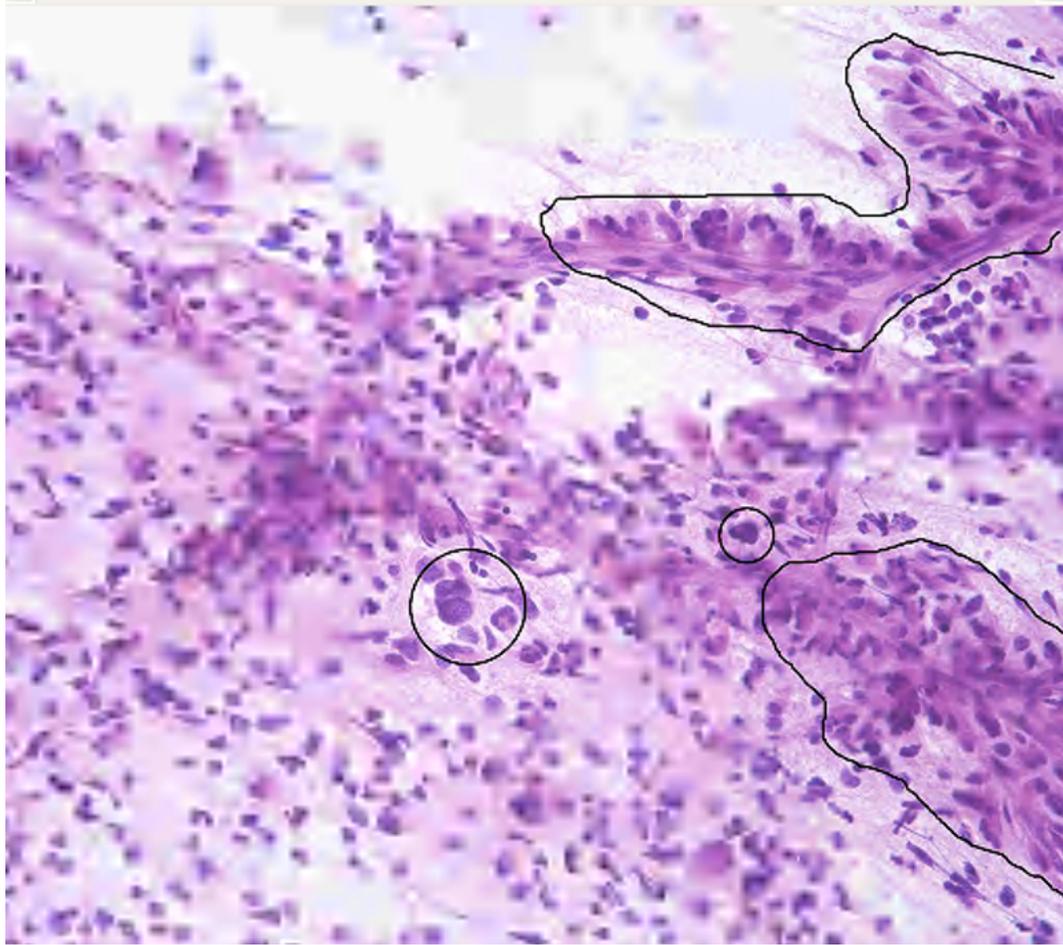


Figure 9: Illustration of ROI based image coding

Since the consulting pathologist is at the other end of the communication link, the ROI is not known to the encoder beforehand. So to facilitate an ROI based compression and transmission, a two-stage process is required. In the first stage, the image is compressed at DL (or a lower bitrate) and is transmitted to the remote client. The pathologist at the remote location then identifies the region of interest using the coarse image information available to him. Once the remotely identified ROI is available at the server, the image is then compressed with the ROI at ML level and the BG at DL level, and then communicated to the client. The two-stage process can be of advantage if the total time spent and the total amount of information communicated

in this forward-reverse exchange is less than that required for a single stage transmission of the image compressed at ML level. This condition can be expressed as follows,

$$\begin{aligned}
 & ML_encode_time + ML_transmit_time \geq \\
 & DL_encode_time + DL_transmit_time + ROI_define_time + \\
 & ROI_receive_time + ROI_encode_time + ROI_transmit_time
 \end{aligned}$$

where, each entry is the time taken to,

$$\begin{aligned}
 ML_encode_time &= \text{encode the entire image at ML} \\
 ML_transmit_time &= \text{transmit the ML-coded image} \\
 DL_encode_time &= \text{encode the entire image at DL} \\
 DL_transmit_time &= \text{transmit the DL-coded image} \\
 ROI_define_time &= \text{locate the ROI} \\
 ROI_receive_time &= \text{receive ROI definition} \\
 ROI_encode_time &= \text{encode the image with ROI} \\
 ROI_transmit_time &= \text{transmit the ROI-coded image}
 \end{aligned}$$

Of the above factors ML_encode_time , DL_encode_time and ROI_encode_time depend on the speed of the chosen compression scheme and the computation resources available at the server side. Also, ROI_define_time depends upon the experience of the remote pathologist, the nature of the slides and other such factors. All the other terms in the above expression depend on the link capacity. Since the aim here is to develop a bitrate budgeting mechanism for telepathology applications subject to bandwidth and latency constraints, other factors depending on the availability of computational resources and human limitations can be cancelled out or ignored for this analysis. Thus a rough upper-bound analysis is possible using the following simplified expression,

$$\begin{aligned}
ML_transmit_time &\geq DL_transmit_time + ROI_receive_time \\
&\quad + ROI_transmit_time
\end{aligned}$$

From the above equation it is obvious that the choice of two-stage transmission or one-stage transmission depends upon the size of the ROI. It is expected that for a small ROI, the savings in the total bitrate for the compressed image due to ROI based compression will be large enough to allow faster transmission at the given line rate. However as the ROI increases the usefulness of the two-stage transmission scheme is expected to diminish.

Another important point to discuss here is the value of using the two-stage transmission scheme. Under feasible conditions the two-stage transmission scheme reduces the size of the total data to be transmitted. This can help in two ways:

1. by *reducing latency*, i.e. reducing the total time required to transmit a diagnostically acceptable image. This is useful in case of delay sensitive applications such as frozen section diagnosis or interactive applications such as remote browsing of whole slide images.
2. by *reducing the time and bandwidth consumption per client*, which allows the transmitter or sever to support larger number of clients simultaneously.

3.2.2 Identifying the interesting cases

As mentioned previously, currently different organizations employ different approaches from telephone lines to dedicated optical links for remote pathology consultation. To evaluate the performance of the proposed two-stage transmission scheme, we need to pick out the interesting cases where the performance of the two-stage and one-stage transmission schemes can be compared. Thus the first step here is to identify bandwidth constraints which are interesting enough to study this problem.

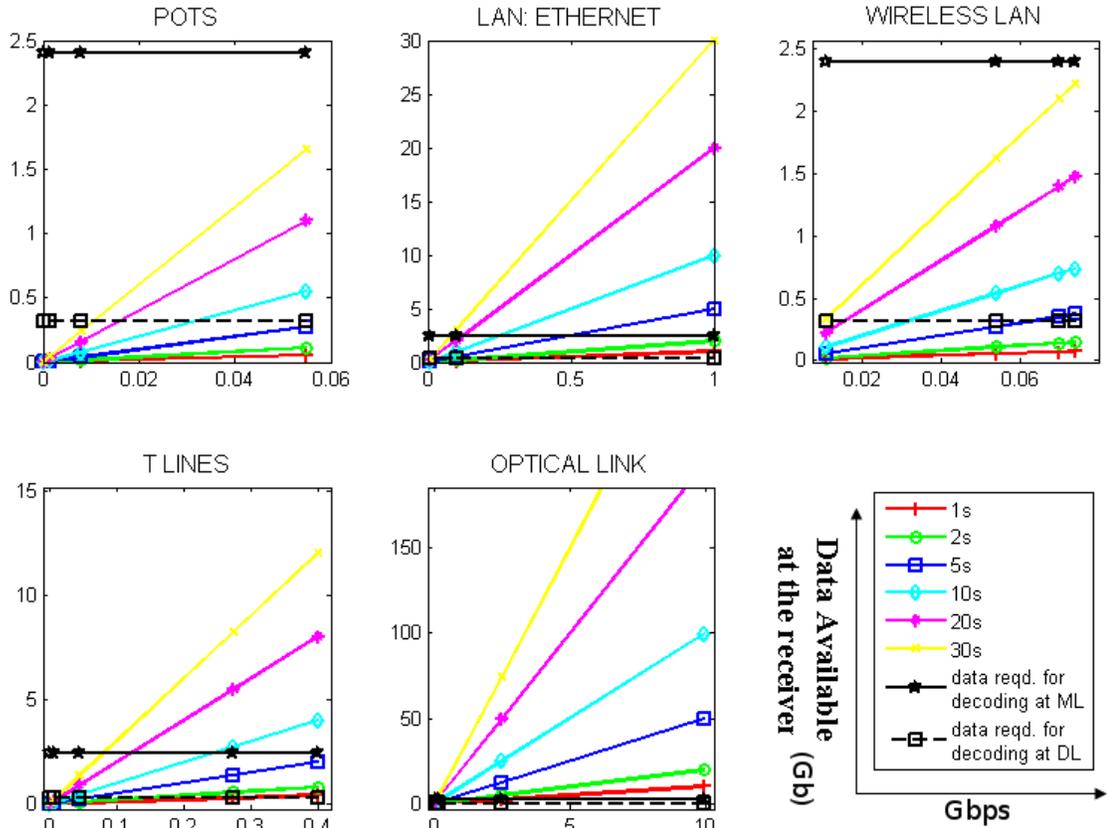


Figure 10: Results of transmitting image compressed at ML over different bandwidths

The plots in Figure 10, which are calculated using simple hand-calculations help us to identify the really interesting scenarios to study the value of multi-stage transmission. The data points on the graphs have been calculated assuming a typical image size of around 200 Mp, which in its uncompressed format (24 bpp) results in 4.8 Gb of data. The lower end of the telepathology bandwidth spectrum employs modems for transmission of images over ordinary telephone lines supporting data rates of around 4.8 Kbps to 56 Kbps. In this case, transmission of the entire image at ML (bpp \approx 12 bpp) or DL (bpp \approx 1.6 to 2.4 bpp) seems impossible if the required delay constraints (say, between 1s to 30s) are to be met. On the other hand, using optical links makes

the image communication problem slightly uninteresting, since at such a high bandwidth (in excess of 1 Gbps) the whole image transmitted at ML without violating even the minimum required delay constraints. However, for the intermediate data rates offered by the Ethernet or the T-carriers, transmission at ML or DL level is not always possible for the given delay constraints. For example using the Fast Ethernet standard and setting the interactive time bound to be around 5s, it is not possible to transmit the image at mathematically lossless level, but possible at the diagnostic lossless level. Similarly by using the T3 lines, image transmission is not possible if the delay target of 5s is to be met, but it is possible by compressing and transmitting at DL level. Thus it seems appropriate to select communication links operating in this bandwidth range for studying the merits of using the two-stage transmission scheme, where ROI will be compressed at ML and BG will be compressed at DL or lower. Moreover, this choice allows us to cover two application domains for a telepathology setup. For consulting pathologists in different departments but residing within the same or nearby hospital buildings (intra hospital scenario), an existing LAN setup over Ethernet can be utilized while long distance, inter hospital remote consultation can be made possible by using the T lines.

3.2.3 One-stage vs. Two-stage transmission

Once the possible transmission scenarios are established we can explore the feasibility of using two-stage transmission while varying the size of ROI. To perform this analysis we need to develop expressions describing the total amount of data exchanged between the server and the clients and the total transmission delay incurred when using the two-stage and the single stage transmission schemes. In the single stage case, the entire image needs to be transmitted at ML level. Hence the total amount of data that needs to be transmitted and the total transmission time is given by,

$$D_{one-stage} = I * R_{ML}$$

$$T_{one-stage} = \frac{D_{two-stage}}{R_{line-rate}}$$

In the above expression,

$D_{one-stage}$ = Total data (bits) that needs to be transmitted in the one-stage case

$T_{one-stage}$ = Total time for image transmission in the one-stage case

I = Image size in terms of the total number of pixels

R_{ML} = Bitrate (bits/pixel or bpp) for Mathematically Lossless compression

$R_{line-rate}$ = Data rate (bits/second or bps) offered by the communication link

Similarly, the expression for the total amount of data ($D_{two-stage}$) that needs to be transmitted, and the total transmission time ($T_{two-stage}$) for the two-stage transmission scheme is as follows,

$$D_{two-stage} = I * R_{DL} + D_{reverse} + I * f * R_{ML}$$

$$T_{two-stage} = \frac{D_{two-stage}}{R_{line-rate}}$$

where,

R_{DL} = Bitrate (bits/pixel or bpp) for Diagnostically Lossless compression

$D_{reverse}$ = Data transmitted by the remote client for defining the ROI

f = Fraction of the image defined as ROI

As mentioned previously, the two stage transmission scheme can be of advantage if the total amount of data that needs to be communicated is reduced ($D_{two-stage} \leq D_{one-stage}$), or the total time for communicating this data is also reduced ($T_{two-stage} \leq T_{one-stage}$). This is expected to happen because,

1. R_{DL} (around 1.6 bpp - 2.4 bpp) is much smaller than R_{ML} (around 12 bpp).
2. The ROI-fraction of image (f) is typically very small and would not occupy more than a quarter of the entire image.
3. If the ROI is a regular shape such as a rectangle or a square, only few bytes of information ($D_{reverse}$) specifying the four corners of the rectangle needs to be communicated in the reverse direction. Even in the case of disconnected or irregular regions of interest, a simple binary mask defining the ROI can be transmitted, resulting in negligible amount of data flow in the reverse direction.

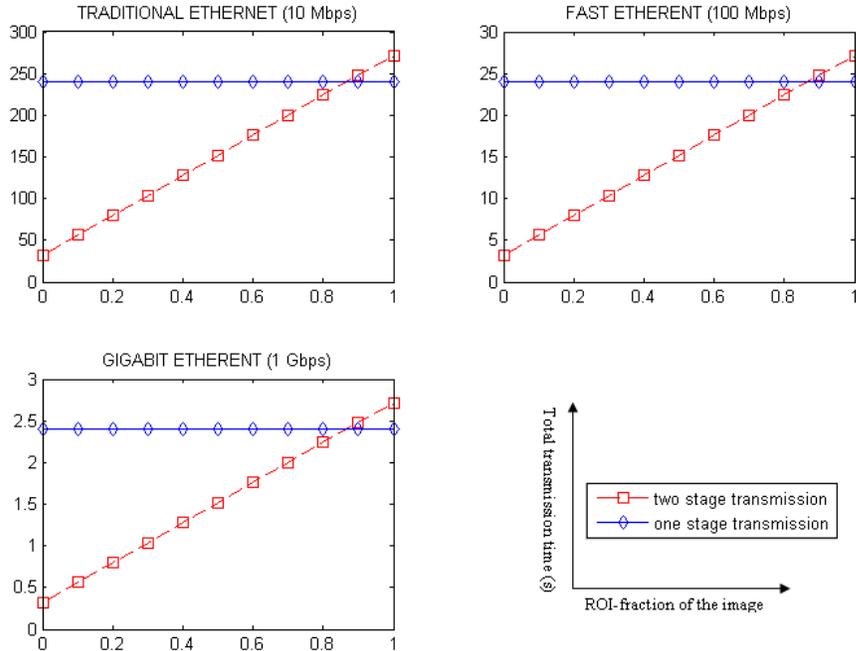


Figure 11: One-stage and two-stage transmission of an image over ETHERNET for varying ROI

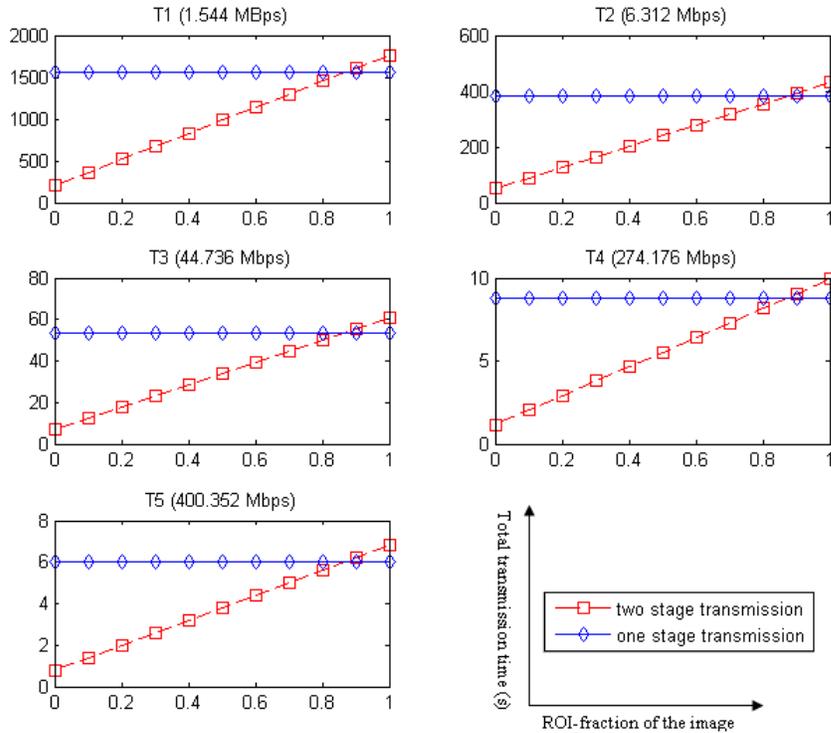


Figure 12: One-stage and two-stage transmission of an image over the T-carriers for varying ROI

Using the above expressions and simple hand-calculations, Figure 11 and Figure 12 were generated. Figure 11 illustrates the transmission delay encountered for the one-stage and two-stage transmission schemes with varying ROI. Here, it is assumed that the data transmitted for the ROI definition in the reverse direction is only around 100-150 bytes. In Figure 11 it is assumed that a local area network employing Traditional, Fast and Gigabit Ethernet is used for transmission. Figure 12 illustrates the same when the T lines are used for transmission. From the two figures we can see that the transmission delay for the two-stage transmission scheme is lower as compared to the one-stage transmission scheme, provided the ROI occupies less than 85 % of the complete image to be transmitted. Typically the region of interest would occupy less than a quarter of an image, and hence a two-stage transmission scheme can be effectively used.

Further, Figure 13 shows the advantage of using a two-stage transmission scheme for supporting multiple clients simultaneously for an ROI which is about 25 % of the image and the maximum allowable transmission time is about 20s. The calculations here assume that there is fair sharing of the available time and bandwidth between all the clients. Clearly more no. of clients can access the image stored on the remote server using a two-stage transmission technique as compared to the one-stage technique.

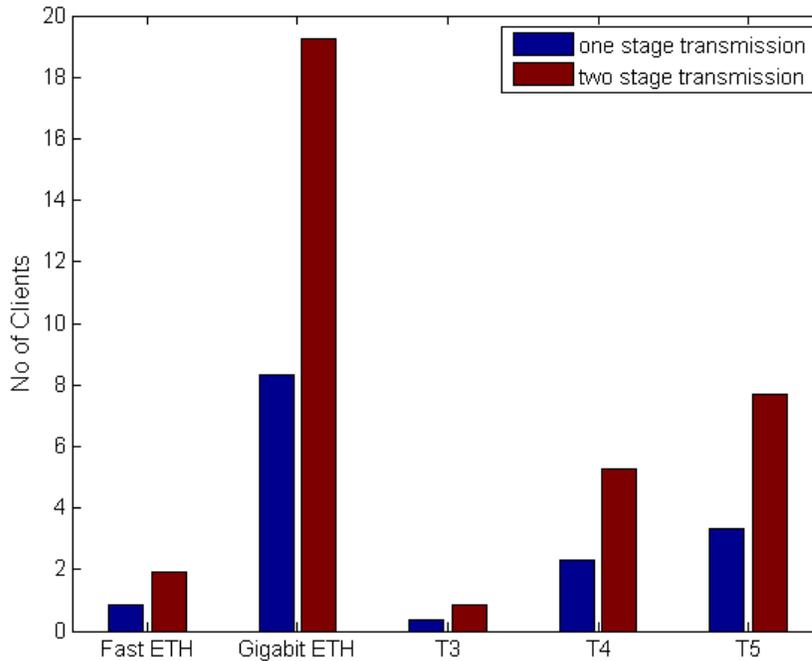


Figure 13: Illustration of number of clients that the server can support simultaneously using one-stage and two-stage transmission schemes

3.2.4 ns-2 simulations

In the previous section we demonstrated the advantage of using a two-stage transmission scheme in place of a one-shot image transmission mechanism using some simple expressions and hand calculated numbers. This analysis can be considered to be extremely optimistic because it ignores some factors and also because it assumes that the entire bandwidth offered by the communication resource is available only

for transmission of useful image data. One way to define the network throughput is that it is *the number of user information bits transmitted per unit time*. In reality, there is a considerable amount of difference between the theoretical line rate and effective user throughput. The effective throughput may drop due to inefficiencies in the implementation of the protocol stack (eg: TCP/IP over Ethernet), the overhead introduced due to the packet headers added along each layer of the protocol stack, due to use of CSMA/CD by the Ethernet MAC, due to non-zero bit-error rate along the channel and many other factors. This throughput loss was not considered in the calculations presented in the previous section. Here, we attempt to perform a more realistic analysis of the problem by using the ns-2 network simulator [34]. In this simulation we set up a LAN based on the Fast Ethernet standard which offers a theoretical line rate of 100 Mbps, and try to determine the feasibility of using a two-stage transmission scheme. In the LAN, one node acts as a server which stores all the digital images while the rest of the nodes behave as clients who have the ability to browse or download these images from the server.

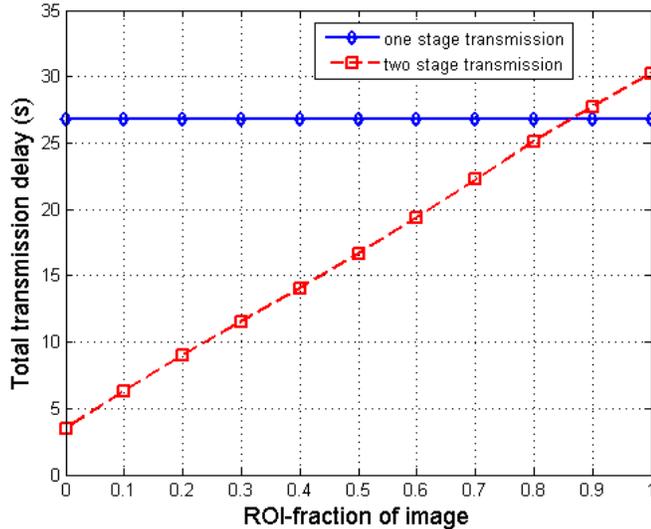


Figure 14: ns-2 simulations illustrating one-stage and two-stage transmission of an image over Fast Ethernet for varying ROI

It is very easy to simulate the behavior of the single stage transmission scheme and determine the average delay experienced by clients for downloading image data from the server. However, ns-2 is a discrete event simulator and hence it is not possible to exactly simulate the real-time, interactive nature of the two-stage transmission scheme which requires forward and reverse communication between the server and the clients. Hence we simulate the problem by allowing the individual Tcl scripts simulating the server-to-client and client-to-server communication to run for a predetermined amount of time, and then aggregating the time-delays experienced for the exchange of desired amount of data along both directions by parsing through the generated trace files offline. Figure 14 shows the total time required for transmitting a 200 Mp image by employing the single-stage transmission scheme and two-stage transmission with varying ROI-size. This figure confirms the results obtained using hand calculations in Figure 11 which stated that for ROI less than 85% of the image the total transmission delay can be minimized by using a two-stage transmission scheme rather than a single stage transmission scheme. The loss of throughput due to a more realistic simulation is also clearly visible from Figure 14, since the transmission time-delays in this case are a bit higher than the theoretical ones. This disagreement between the theoretical and actual delays is expected to increase as more number of clients contend for the shared resource.

The hand-calculated and simulation results indicate that due to the sheer size of the digital pathology images, the desired interactive time-bounds are not easily met in spite of using the two-stage transmission scheme and Fast Ethernet. Thus further innovations are necessary to address this challenge of compression and transmission of digital pathology images.

3.3 Future Work: Eliminating the bottleneck in the two-stage transmission scheme

In the previous section we analyzed the merits of using a two-stage transmission scheme for time-sensitive telepathology applications. In that analysis we chose to ignore the human factor, consisting of the time consumed by the pathologist to identify the ROI. If this time is taken into consideration the total time for the two-stage transmission scheme could exceed that of the one-stage transmission scheme. This by no means voids the usefulness of the two-stage transmission scheme, since we would still be transmitting less amount of data in the two-stage transmission scheme, thereby reducing the channel bandwidth and time consumed by each client. However having to wait for the ROI definition from the remote pathologist presents a major bottleneck for the two-stage transmission scheme. In this section we will discuss some efforts that could help to remove this bottleneck.

The easiest way to remove the pathologist from the image transmission process is by developing automatic methods to determine the possible regions of interests at the server/encoder side. If the ROI definition is available to the encoder then the two-stage transmission scheme reduces to a simple single stage transmission scheme, where the predetermined ROI is compressed at ML level and the BG is compressed at DL or lower level. In [27] the raw digitized slide is first annotated to identify diagnostically interesting regions which are then compressed at ‘visually lossless’ compression levels. Regions identified as containing non-salient information are compressed lossily and then the compressed image is transmitted. The limitation of this work is that the ROI needs to be identified manually by a pathologist at the transmitter side. The content based image compression scheme proposed in [14] consists of a two-stage process: image content analysis and image encoding. In the first stage, several steps such as texture analysis, histogram based segmenting, morphological processing etc. are taken to automatically segment the interesting objects in the image. Once the

image is partitioned into regions, it is encoded using a wavelet based compression scheme, where the objects/ regions of interest get coded at higher bitrates.

Since radiology images constitute the most dominant class of digital medical images several methods/software are available for ROI-based compression [43] and image segmentation [58], which can locate the diagnostically important regions in radiology images. However there is big difference in the nature of digital radiology and digital pathology images. Radiology images are grayscale, while pathology images are necessarily color images; typically represented with 24 bpp (2^{24} different colors). The properties of the diagnostically important features such as the myocardium in a cardiac MRI for radiology images are much different than the properties of the diagnostically important features in pathology images such as nuclei possessing atypical shapes or colors. Hence the image segmentation, compression and transmission techniques which are commonly used for digital radiology images cannot be directly imported to the telepathology domain.

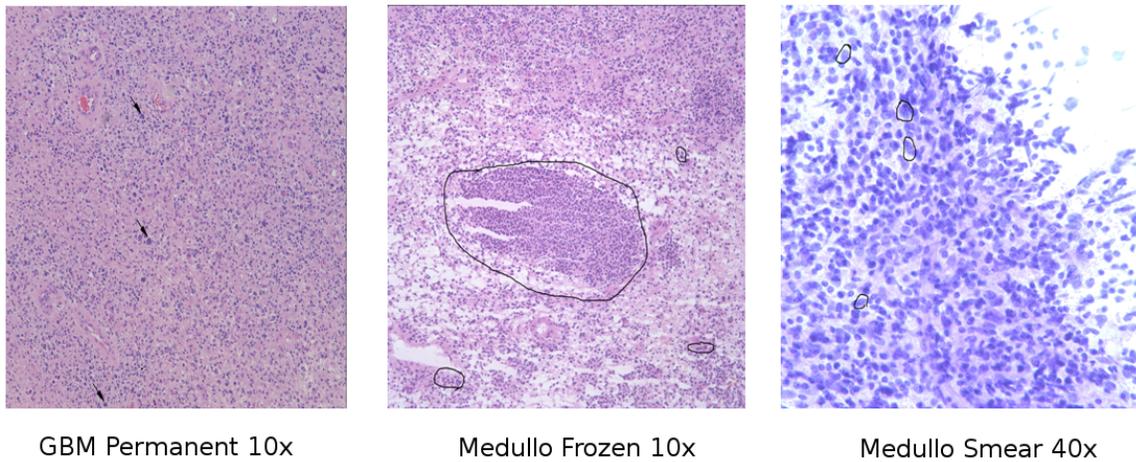


Figure 15: Annotated images illustrating the interesting features in smears, permanent and frozen section digital pathology images

Identifying all the interesting regions in a pathology images is not a trivial problem. Two factors that contribute to the complexity of this problem are: a) there is

considerable amount of inter and intra-pathologist discordance regarding what can be considered as ROI/non-ROI, b) the characteristics describing the diagnostically important features within the slide are not consistent for different types of pathology images. Figure 15 illustrates the diagnostically important features which were hand-annotated by a pathologist. As seen from Figure 15 there is no consistency with respect to the size, shape, texture or color of the regions identified as ROI for different types of pathology images such as smears, permanent or frozen sections. Clearly developing an automatic segmentation technique which would accurately identify all the diagnostically important regions in the image, for all different types of pathology images is a very challenging task. Also the penalty of wrongly classifying a ROI as BG is very high, since the BG would be subsequently compressed at very low bit-rates. We were able to locate a very limited number of articles which attempt to automatically segment the ROI in pathology images [1, 5, 9, 42, 61]. Most of these techniques roughly follow the following steps:

1. *Color space transformation* : The RGB image is transformed to HSI, HSV or other color spaces [5] which facilitate easier segmentation.
2. *Segmentation* : The image is then segmented using global/adaptive thresholding [61] followed by edge [1] or contour detection or partitioned into *clusters* using the k-means [42], the mean shift [9] or other such methods.
3. *Post-processing* : The segmented or clustered images is then subject to morphological operations [1] such as opening, convex hull etc. are to remove any holes within the detected objects. Noise or false positives are filtered out based on their shape or size properties.

We implemented some variants of the approaches mentioned above. As expected, we found that none of the approaches seemed to work perfectly for all types of images (smears, frozen and permanent sections) in our database. Figure 16 shows the results

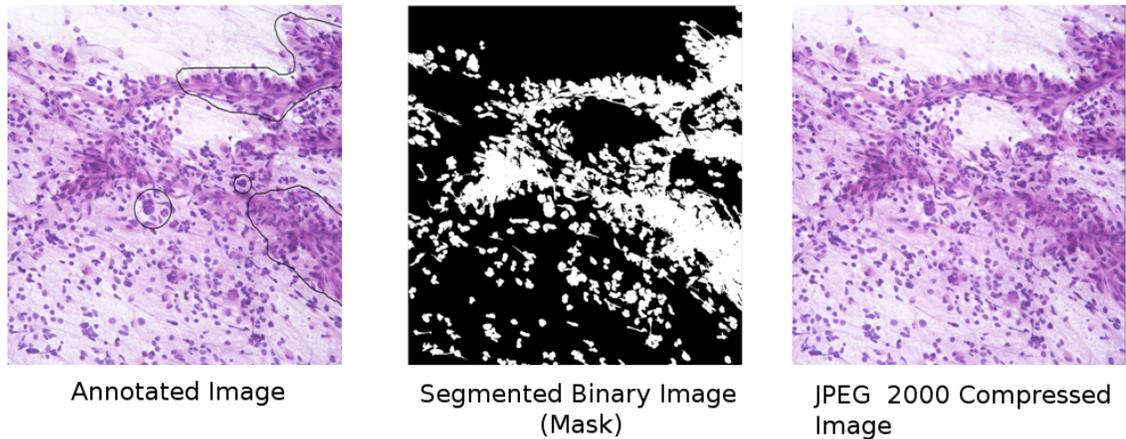


Figure 16: Preliminary results demonstrating automatic ROI detection

from one of our implementations, where we segmented the image in the HSI color space, used the k-means clustering algorithm to partition the image and then perform morphological opening and area-based object filtering to reduce the number of false positives. As seen from Figure 16 all the annotated features were tagged as ROI along with some false positives which were not filtered out during the post-processing stage. The binary mask image obtained as an output of the automatic segmentation procedure is then used to perform ROI-based compression using JPEG 2000. The image is compressed at a compression ratio of around 70:1 and PSNR of around 32 dB. The image needs to be inspected at its full spatial resolution on the computer monitor to spot the perceptual differences between the original and the compressed image and between the ROI and the BG. After experimenting with a few algorithms we concluded that currently there is no ‘silver-bullet’ solution which facilitates automatic segmentation of all the diagnostic features within all the different classes of pathology images. Thus there is a substantial scope for future research along this direction.

CHAPTER IV

CONCLUSION

This thesis identified and addressed the two technology challenges in telepathology: compression and transmission of digital pathology images. We addressed these two challenges as follows,

1. **Choosing suitable compression ratios and compression algorithms :**

We conducted subjective tests to determine the maximum possible compression ratio while preserving the diagnostic accuracy of pathology images, and observed that *diagnostic losslessness* could be achieved for compression ratios as high as **10:1** to **20:1**. We also set up subjective tests to evaluate and compare images compressed using the JPEG and the JPEG 2000 algorithms, which are commonly used for compression of medical images. Our results indicated that for low and moderate bitrates (0.2 bpp to 0.55 bpp) JPEG 2000 is the clear winner, while at higher bitrates (≥ 0.65 bpp) the images compressed using the JPEG and the JPEG 2000 algorithms appear to be visually indistinguishable.

2. **Employing a two stage transmission scheme for transmission of rich**

pathology images : We proposed and evaluated the merits of using a *two-stage transmission scheme*, where coarse image information compressed at diagnostically lossless (or lower) level is sent to the client(s) at the first stage, and the Region of Interest (ROI) details are transmitted at mathematically lossless compression level at the second stage. We concluded that if the area occupied by the ROI is less than 85% of the image, it is advantageous to use the two-stage transmission scheme instead of transmitting the entire image in a single shot.

In summary, we identified that due to the sheer size of the digital pathology images, implementing a low-latency telepathology system which allows communication of rich images with sufficient diagnostic accuracy presents some significant challenges. Although these challenges were by no means entirely solved, we were successful in achieving substantial improvements by introducing some amount of *intelligence* in the image compression and transmission aspects of telepathology.

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