

الجمهورية الجزائرية الديمقراطية الشعبية
People's Democratic Republic of Algeria
وزارة التعليم العالي و البحث العلمي
Ministry of Higher Education and Scientific Research



Mohamed Khider University Biskra
Faculty of Science and Technology
Department of Electronic Engineering
Section: Electronic
Option: Telecommunication

Ref:

**Memory of end study
for Graduation of:**

MASTER

Theme

***Nonlinear Detection of Lesion with ANOVA Technique
For Multi MRI images***

Presented by:

KHELIL Seif eddine

Stands for: June 2nd, 2014

In front of the jury:

Dr. Fedias Meriem

M.C.B

President

Dr. El Kourd Kaouther

M.C.A

Supervisor

Dr. Dhiabi Fathi

M.A.B

Examinator

University of the year: 2013 / 2014

الجمهورية الجزائرية الديمقراطية الشعبية
People's Democratic Republic of Algeria
وزارة التعليم العالي و البحث العلمي
Ministry of Higher Education and Scientific Research



Mohamed Khider University Biskra
Faculty of Science and Technology
Department of Electronic Engineering
Section: Electronic
Option: Telecommunication

**Memory of end study
for Graduation of:**

MASTER

Theme

*Nonlinear Detection of Lesion with ANOVA Technique
For Multi MRI images*

Presented by:

Name

Favorable opinion of the supervisor:

Name

Signature

Favorable opinion of the President of Jury

Name

Signature

Stamp and Signature

الجمهورية الجزائرية الديمقراطية الشعبية
People's Democratic Republic of Algeria
وزارة التعليم العالي و البحث العلمي
Ministry of Higher Education and Scientific Research



Mohamed Khider University Biskra
Faculty of Science and Technology
Department of Electronic Engineering
Section: Electronic
Option: Telecommunication

Theme :

Nonlinear Detection of Lesion with ANOVA Technique For Multi MRI images

Offered by:

Directed by:

Abstract

In our work, we begin by translating a non linear model to linear one by using the numerical analysis with Runge-Kutta4 (*RK4*).

After that, we pass to the statistical study for *linear regression* then for the analysis of variance, “*ANOVA* technique”, by applying the statistical study on the pathological image to detect the tumors of *multi MRI* images.

In the last, we compare the result obtained for nonlinear model with linear one.

ملخص

في عملنا هذا، نبدأ بترجمة وتحويل نموذج غير خطي إلى آخر خطي باستخدام التحليل العددي مع (*RK4*). بعد ذلك نمر إلى دراسة إحصائية عن الانحدار الخطي ثم تحليل التباين، تقنية الـ“*ANOVA*”، من خلال تطبيق الدراسة الإحصائية على الصورة المرضية للكشف عن الأورام من صور الرنين المغناطيسي المتعددة واستخراج مكان الأفة.

ثم أخيرا نقوم بمقارنة النتائج المتحصل عليها من النموذج الغير خطي مع النموذج الخطي.

Dédicace

I dedicate this modest work;

To my parents; my man that am looking for, my eternal example, my moral support and my source of efforts, who has always sacrificed to see me succeed, to you my Father.

To the light of my life, the source of my joy and happiness, the flame of my heart, my life; Mom that I love

No tribute could be worthy of the love that they constantly fill me with. God bless them

To the people that I like and need their presence in my life, to my brother & my best friend Youcef (Jo), to all my sisters; Amina (Mina), Dounia (Doudi), and my dear Jouhaina (JOJO), without forgetting to mention my Grandmother which is to me a second Mum (Omma) and for that I thank Allah, may God gives her a good health and a long life. I dedicate this work with great pleasure, to their returns primarily for their advices, supports, and encouragements.

To the people who have always helped and encouraged me, who were always by my side, and who accompanied me during my graduate path, my kind friends, colleagues study and brother heart; Rahim.

KHELIL Seif eddine

Acknowledgment

First of all, I want to thank Allah the Almighty for giving me health and willingness to initiate and complete this memory.

Second of all, this work would not be as rich and would not have been possible without the assistance and guidance of my supervisor "Dr. Elkourd Kaouther", for that I thank her for the quality of her exceptional leadership, for her patience, rigor and availability during our preparation of this modest work,

I thank all the members of the jury; they have agreed to consider and evaluate this work,

My deepest thanks go to my dear friend "Ahlem" for her practical help, moral support and encouragement.

I also thank my brother "Youcef" for his help, my entire family for the support and all those who helped and sustained near or far.

In the last, I thank all the teachers in the electronics department for their great efforts, generosity and patience that they have demonstrated despite their busy academic and professional program.

List of tables

CHAPTER III: Theoric of numerical and statistical methods

Tab. III.1 ANOVA summary table	62
Tab. III.2 ANOVA table for simple linear regression	62

CHAPTER IV: Conception & Results

Tab. IV.1 Comparison between our & previous ANOVA projects.....	80
---	----

List of figures

CHAPTER I: Principles of digital image

Fig. I.1 Digital image from analog image	5
Fig. I.2 Shows relationship between an analog image and a digitized image	6
Fig. I.3 Classification of quantizer	7
Fig. I.4 Digital image representation	8
Fig. I.5 Binary image representation	10
Fig. I.6 Mother Teresa in black and white.....	10
Fig. I.7 Grayscale image representation	11
Fig. I.8 Mother Teresa in grayscale.....	11
Fig. I.9 RGB image representation.....	12
Fig. I.10 Kalpana chawla's colour image.....	12
Fig. I.11 Cross-section through a typical human eye.....	13
Fig. I.12 Structure of the photoreceptors of the human eye.....	14
Fig. I.13 Spectral sensitivity of the rods and cones.....	14
Fig. I.14 DICOM Application Entities.....	16
Fig. I.15 Comparison of file sizes for different image types, file types, and compression methods.....	19

CHAPTER II: Fundamentals of medical imaging

Fig. II.1 A standard x-ray tube	22
Fig. II.2 A typical X-ray radiographic geometry.....	23
Fig. II.3 Computed radiography detectors.....	24
Fig. II.4 Digital radiography image detectors.....	24
Fig. II.5 Posterior–anterior chest radiographs	25

List of figures

Fig. II.6 Modern fluoroscopy.....	26
Fig. II.7 Fluoroscopic examination of the GI tract with contrast agent.....	27
Fig. II.8 A modern CT scanner.....	28
Fig. II.9 The seven generations of CT scanners	29
Fig. II.10 Contrast enhanced CT images	30
Fig. II.11 Mammographic imaging.....	32
Fig. II.12 (i) Normal breast.....	32
Fig. II.13 A typical US beam.....	34
Fig. II.14 Ultrasound imaging	35
Fig. II.15 Ultrasound images of carotid artery	36
Fig. II.16 Two transverse slices of the same patient	37
Fig. II.17 In a superconducting MRI device.....	38
Fig. II.18. Nuclear magnetic resonance	39
Fig. II.19 simplest kind of fMRI experiment.....	39
Fig. II.20 The complete spin-relaxation family tree	40
Fig. II.21 T1 and T2 weighted spin echo image of the head	40
Fig. II.22. High resolution saggital MRI brain image	41
Fig. II.23 Relative contributions from natural background, medical, and other sources	41
Fig. II.24 Sequence of events in the radiation damage in cells	42

CHAPTER III: Theoric of numerical and statistical methods

Fig. III.1 Runge's motivation	47
Fig. III.2 Comparison of Runge-Kutta methods of 1st (Euler), 2nd , and 4th order	54
Fig. III.3 Points corresponding to observations from the simple linear regression model... 55	55
Fig. III.4 An F curve and critical value $F\alpha, v_1, v_2$	61

CHAPTER IV : Conception & Results

Fig. IV.1 Global flow chart 67

Fig. IV.2 Analysis of flow chart 68

Fig. IV.3 MRI scan 69

Fig. IV.4 Choosing samples of images with automatic detection 70

Fig. IV.5 Matlab code of nonlinear model 71

Fig. IV.6 Plotting the first vectors of matrixes (normal & pathological image)..... 71

Fig. IV.7 Display the image for each matrix by two ways (before & after used *RK4*) 72

Fig. IV.8 Presentation of image after used *RK4* with variation of the step size *H*..... 72

Fig. IV.9 Presentation of the error *e*, *y* & *y* for both curves. 73

Fig. IV.10 Detect the lesion with two ways 74

Fig. IV.11 Comparison between nonlinear model & linear one..... 76

Fig. IV.12 Comparison (“length of image”)..... 76

Fig. IV.13 Comparison (“number of image”)..... 77

Fig. IV.14 Comparison (“detection of tumor zone”)..... 77

Fig. IV.15 Comparison (“execution time”) 78

Fig. IV.16 Interface system.....79

Abbreviation list

2D: Bidimensional

3D: Tridimensional

RGB: Red, Green and Blue

HSV: Hue, Saturation, Value

CMYK: Cyan, Magenta, Yellow, Black

HVS: Human visual system

FOV: Field of view

DPI: Dot per inch

DICOM: Digital imaging and communications in medicine

JFIF: JPEG file interchange format

GIF: The graphic interchange format

PNG: The portable network graphics

TIF or TIFF: The tagged image file format

BMP: Bitmaps

LZW: Lempel-ziv-welch

eV: electron-Volt

CCD: Charge-coupled device

X-ray: X-rays, γ -rays (energies above ≈ 10 keV)

MRI: Magnetic resonance image

US: Ultrasound

NMR: Nuclear resonance image

FID: Free induction decay

fMRI: Functional MRI

Abbreviation list

CT: Computed tomography

CR: Computed radiography

DR: Digital radiography

RF: Radiofrequency

CMOS: Complementary metal semiconductor

II: Image intensifier

TE: Echo time

TR: Repetition time

ANOVA: Analysis of variance

RK4: Runge-Kutta 4

df: Degree of freedom

SSTr: Sum of squares treatment

SSE: Sum of squares error

SST: Total sum of squares

SSR: Sum of squares regression

Abstract

In our work, we begin by translating a non linear model to linear one by using the numerical analysis with Runge-Kutta 4 (**RK4**), this method is the most popular where The step size H is working to increase the lighting of the image compared with the original picture.

After that, we pass to the statistical study for **linear regression** then for the analysis of variance, "**ANOVA** technique", by applying the statistical study on the pathological image to detect the tumors of **multi MRI** images and extract the place of lesion by two ways: distribution of Gaussian curve (hypothesis test of h_0) and directly on the pathological image.

And last but not least, we compeer the result obtained for nonlinear model with linear one.

Keywords: RK4, Linear Regression, ANOVA technique, Tumors, Multi MRI images.

ملخص

في عملنا هذا، نبدأ بترجمة وتحويل نموذج غير خطي إلى آخر خطي باستخدام التحليل العددي مع (RK4)، وهذه الطريقة هي الأكثر شعبية حيث يعمل حجم الخطوة H على زيادة الإضاءة للصورة مقارنة مع الصورة الأصلية.

بعد ذلك، نمر إلى دراسة إحصائية عن الانحدار الخطي ثم تحليل التباين، تقنية الـ "ANOVA"، من خلال تطبيق الدراسة الإحصائية على الصورة المرضية للكشف عن الأورام من صور الرنين المغناطيسي المتعددة واستخراج مكان الآفة بطريقتين : توزيع منحني "Gaussian" (اختبار فرضية H_0) ومباشرة على الصورة المرضية.

ثم أخيرا وليس آخرا، نقوم بمقارنة النتائج المتحصل عليها من النموذج الغير خطي مع النموذج الخطي.

كلمات دلالية: RK4، الانحدار الخطي، تحليل التباين "ANOVA"، الأورام، صور الرنين المغناطيسي المتعددة.

Table of contents

General Introduction: Background and Objectives..... 1

CHAPTER I: Principles of digital image

I.1 Introduction:..... 5

I.2 Image: 5

 I.2.1 Analog Image: 5

 I.2.2 Digital image: 5

I.3. Digitizing an image:..... 6

 I.3.1 Image sampling: 7

 I.3.2 Quantization: 7

I.4 Image information:..... 7

 I.4.1 Digital image representation: 8

 I.4.2 Pixels: 8

 I.4.3 Volume image: 9

 I.4.4 Image Size, Scale, and Resolution: 9

 I.4.5 Image types: 10

 I.4.5.1 Binary images: 10

 I.4.5.2 Grayscale image: 11

 I.4.5.3 Color image: 11

 I.4.6 The quality of a digital image: 12

I.5 Imaging systems: 13

 I.5.1 The human visual system: 13

 I.5.2 Anatomy of the human visual pathway:..... 13

Table of contents

I.6 Image storage:.....	15
I.6.1 Image file format:.....	15
I.6.2 What is DICOM?	16
I.6.3 Image Data Compression Methods:.....	17
I.6.4 Which method is best?	18
I.7 Conclusion:	19

CHAPTER II: Fundamentals of medical imaging

II.1 Introduction:	21
II.2 Medical imaging modalities:	21
II.2.1 Medical images obtained with ionizing radiation (X-rays imaging):.....	22
II.2.1.1 X-ray radiography: The first revolution.....	23
II.2.1.2 X-ray fluoroscopy:	25
II.2.1.3 X-ray CT: The second revolution.....	27
II.2.1.4 X-ray mammography:	31
II.2.2 Medical images obtained with non-ionizing radiation:	33
II.2.2.1 Ultrasound imaging (US):.....	33
II.2.2.2 Magnetic resonance imaging (MRI):	36
II.3 Our exposure to ionizing Radiation:.....	41
II.4 Conclusion:.....	43

CHAPTER III: Theoric of numerical and statistical methods

III.1 Introduction:.....	45
III.3 The Runge-Kutta methods:	48
III.3.1 Basic Runge-Kutta methods:.....	48
III.3.2 Fourth-order Runge-Kutta method:.....	48
III.3.3 Runge-Kutta for coupled systems (two-variables):.....	49

Table of contents

III.3.4 Examples:	50
III.4 Regression analysis:	54
III.4.1 The two-variable linear model:.....	54
III.4.2 The ordinary least-squares method:.....	55
III.4.3 Test of goodness of fit and correlation:	56
III.5 Review of the R. A. Fisher's Statistical Methods for Research Workers:.....	58
III.6 Understanding the analysis of variance:.....	58
III.6.1 Basics of ANOVA:	58
III.6.2 The null hypothesis:.....	59
III.6.3 The assumptions of ANOVA:	59
III.6.4 Calculating SS_{total} , $SS_{treatment}$, and SS_{error} :.....	59
III.6.5 Degrees of freedom:	60
III.6.6 Mean squares:	61
III.6.7 The F test:	61
III.6.8 ANOVA summary table:	62
III.7 Regression ANOVA: the other way to understand the basic logic:.....	62
III.8 Conclusion:.....	62

CHAPTER IV : Conception & Results

IV.1 Introduction:.....	64
IV.2 Computer Identification:	64
IV.3 What is Matlab?	64
IV.4 Magnetic resonance imaging (MRI):	65
IV.5 EXPERIMENTAL RESULTS	67
IV.5.1 Global <i>flow chart</i> :.....	67
IV. 5.2 Analysis of <i>flow chart</i> :	68
IV.5.3 Analysis of data (the protocol radiologic):.....	69

Table of contents

IV.5.4 Choosing samples of <i>MRI</i> images (multi) with automatic detection:	69
IV.5.5 Analysis of RK4:	71
IV.5.6 Calculation of the error between “y” and fitted regression line:	73
IV.5.7 Calculation of the statistic:	74
IV.5.8 Comparison between Anova with <i>RK4</i> and without it:	75
IV.6 What makes my work special than others done before? (Comparison).....	76
IV.7 Conclusion:	80
Conclusion & Perspectives:	81
Bibliographies:	83

Introduction

Background and Objectives

Digital imaging or **digital image acquisition** is the creation of digital images, typically from a physical scene. The term is often assumed to imply or include the processing, compression, storage, printing, and display of such images. The most usual method is by digital photography with a digital camera but other methods are also employed.

Digital imaging was developed in the 1960s and 1970s, largely to avoid the operational weaknesses of film cameras, for scientific and military missions including the KH-11 program. As digital technology became cheaper in later decades, it replaced the old film methods for many purposes. [1]

Most of the attributes of digital images and the methods of image processing introduced in this text originate from outside of medicine. We can single out medical imaging for special consideration because the lives of people often depend on correct acquisition, processing, and interpretation of medical images. [2]

Until 1896 no means existed to examine or measure the hidden internal world of the living human body. Roentgen's discovery of the penetrating X-ray, in 1896, started a revolution in medical imaging and began a slow process of reunification of medical science with physics, chemistry and engineering, the so-called exact sciences.

Medical imaging systems detect different physical signals arising from a patient and produce images. An imaging modality is an imaging system which uses a particular technique. Some of these modalities use ionizing radiation such as radiography, CT scanner and mammography, radiation with sufficient energy to ionize atoms and molecules within the body, and others use non-ionizing radiation. Ionizing radiation in medical imaging comprises x-rays and γ -rays, both of which need to be used prudently to avoid causing serious damage to the body and to its genetic material. Non-ionizing radiation, on the other hand, does not have the potential to damage the body directly and the risks associated with its use are considered to be very low. Examples of such radiation are ultrasound (US), i.e. high-frequency sound, and radio frequency waves are magnetic resonance image (*MRI*).

General Introduction

From about the time of Newton onwards, the exact sciences were able to make very rapid progress in both experimental technique and the establishment of approximate mathematical laws governing the behavior of inanimate nature. The mathematical models, although beautiful and deserving of study in their own right, owe their importance to their power of prediction. Whether it is numerical analysis, regression analysis, the statistical study using analysis of variance, or more briefly *ANOVA*, precise physics and engineering recipes can be looked up or deduced which allow a paper calculation to predict in great detail what the real object will do. The success arises from the well-established underlying unity of the theory and the relative simplicity and reproducibility of the inanimate natural world. Medical Science could not match this progress because the available scientific instruments were incapable of isolating simple general principles from the very much more complex behavior of biological matter. Whereas the exact sciences now rest entirely on unified underlying mathematical theories, medical science is still largely empirical in its approach. Today science and medicine are popularly seen as two separate disciplines, attracting two somewhat different types of scientist. [3]

The subject inter into actual topics, which help doctors to detect the smallest lesions by using statistical methods with Anova one way for non linear model with applied *RK4* [4][5], this method is most popular and a good choice for common purposes because it is quite accurate, stable, and easy to program. The fourth-order Runge-Kutta method requires four evaluations of the righthand side per step h .

The new work in front of the precedent memory or research is applied Runge-Kutta 4 for multi images in short time.

As problematic, what are the principles of digital image and fundamentals of medical imaging? What is the relationship between the two of them? What's the meaning of Runge kutta? What it the result of it? What's the main of the regression and how do we pass to Anova technique? What's the relation between theoric result of Anova (f_{cal}) & Anova table (f_{tab})?

All these questions will be more explain in our work, which is organized as follows:

✚ The first part is a state of the art consists of two chapters:

In the first chapter, we define the digital image and corresponding principles; image information, digitizing an image and the quality of it, image file formats... etc.

General Introduction

In the second chapter, we present a few of the features of a good introductory of medical imaging and its fundamentals, then we briefly introduce its modalities such as Radiography, CT scanner, US, MRI...etc.

✚ The second part, also consist of two chapters:

In the third chapter, we study methods and techniques based on numerical analysis with Runge-Kutta 4, it's mathematical solutions to study the approximation's solutions of ordinary differential equations, also based on linear regression with least square method that gives the best fitted line and last but not least based on statistical study using the analysis of variance "ANOVA".

The last chapter concerning the design and implementation of our system which consist of:

Chapter design in which we describe the design of our system by an overall architecture that highlights the different components and their relationships, then we present the functional aspect in the detailed design.

References used during preparing our project:

- ✓ K.el kourd, "Detect the Tumor with Numerical Analysis and With "ANOVA" Technique for MRI Image", International Journal of Engineering and Innovative Technology (IJEIT), Volume 3, Issue 1, July 2013, ISSN: 2277-3754 ISO 9001:2008 Certified, Florida, pp: 257-260, impact factor. 1.895
- ✓ K. elkourd, "Linearization of exponential model to extract the lesion from pathological image of MRI with two techniques STUDENT & FISHER", Computer Applications & Technology, (ICAAT), july, 2012, pp: 39-43.
- ✓ K.el kourd, " The detection of disease by statistic test of "analyze of variance", Computer Applications & Technology , 20 Jan. 2013 , IEEEExplore, ISSN:978-1-4673-5284-0,pp:1-6

During prepared this subject we have only one difficulty which is; doing the stage for understanding more principles about *MRI* machine.

CHAPTER I

Principles of digital image

I.1 Introduction:

Digital images play an important role, both in daily-life applications such as satellite television, magnetic resonance imaging, computer tomography as well as in areas of research and technology such as geographical information systems and astronomy. An image is a 2D representation of a three-dimensional scene. A digital image is basically a numerical representation of an object. The term digital image processing refers to the manipulation of an image by means of a processor. The different elements of an image-processing system include image acquisition, image storage, image processing and display. This chapter begins with the basic definition of a digital image and is followed by a detailed discussion on two dimensional sampling. This is followed by different elements of image processing systems. [6]

I.2 Image:

An image is a two-dimensional function that represents a measure of some characteristic such as brightness or color of a viewed scene. An image is a projection of a 3D scene into a 2D projection plane. It can be defined as a two-variable functions, $f(x,y)$ where for each position $f(x,y)$ in the projection plane, $f(x,y)$ defines the light intensity at this point. [6]

I.2.1 Analog Image:

An analog image can be mathematically represented as a continuous range of values representing position and intensity. An analog image is characterized by a physical magnitude varying continuously in space. For example, the image produced on the screen of a CRT monitor is analog in nature. [6]

I.2.2 Digital image:

A digital image is composed of picture elements called pixels. Pixels are the smallest sample of an image. A pixel represents the brightness at one point. Conversion of an analog image into a digital image involves two important operations, namely, sampling and quantization, which are illustrated in Fig. I.1

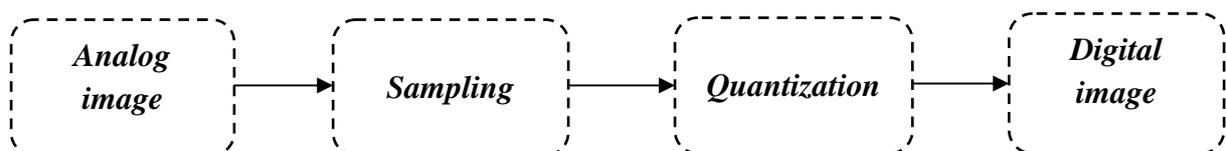


Fig. I.1 Digital image from analog image [6]

Advantages of Digital Images The advantages of digital images are summarized below:

- ✓ The processing of images is faster and cost-effective.
- ✓ Digital images can be effectively stored and efficiently transmitted from one place to another.
- ✓ When shooting a digital image, one can immediately see if the image is good or not.
- ✓ Copying a digital image is easy. The quality of the digital image will not be degraded even if it is copied for several times.
- ✓ Whenever the image is in digital format, the reproduction of the image is both faster and cheaper.
- ✓ Digital technology offers plenty of scope for versatile image manipulation.

Drawbacks of Digital Images Some of the drawbacks of digital image are given below:

- ✓ Misuse of copyright has become easier because images can be copied from the Internet just by clicking the mouse a couple of times.
- ✓ A digital file cannot be enlarged beyond a certain size without compromising on quality.
- ✓ The memory required to store and process good-quality digital images is very high.
- ✓ For real-time implementation of digital-image-processing algorithms, the processor has to be very fast because the volume of data is very high. [6]

I.3. Digitizing an image:

We have discussed some of the advantages of digital images, including easy storage and post-processing. If an image is analog, for example a film radiograph, it can be digitized to obtain a digital image; the same considerations apply in mapping a real object directly to a digital image. There are two steps involved: spatial quantization and intensity quantization. The term quantization means that a variable is not allowed to take any value, but can only take certain allowable (quantized) values; for example, only integer values but not the non-integer values between them. [7]

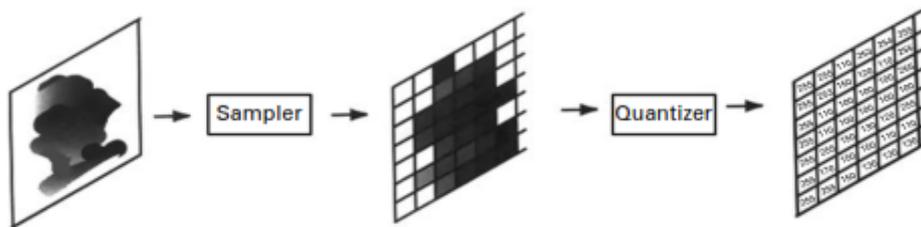


Fig. I.2 Shows relationship between an analog image and a digitized image. [7]

I.3.1 Image sampling:

Sampling is the process of measuring the brightness information only at a discrete spatial location. A continuous image function $f(x,y)$ can be sampled using a discrete grid of sampling points in the plane. [7]

I.3.2 Quantization:

Quantization involves representing the sampled data by a finite number of levels based on some criteria such as minimization of quantizer distortion. Quantizer design includes input decision level, output representation level and the number of levels. Quantizers can be broadly classified into two types, namely, scalar quantizers and vector quantizers. The classification of quantizers is shown in Fig. I.3

Examples of uniform scalar quantizers are midtread and midrise quantizers. An example of a non-uniform scalar quantizer is the Lloyd-Max quantizer. [6]

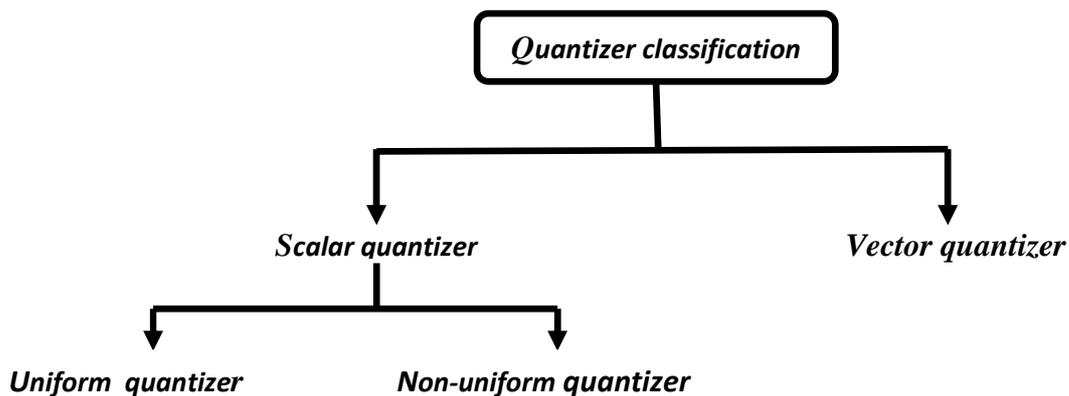


Fig. I.3 Classification of quantizer [6]

I.4 Image information:

It should now be quite clear that because digital images are so easily stored, transmitted, and displayed on different media the physical form of a specific digital image is highly context-dependent. Much more significant than the physical form of a digital image is its information content. The maximum amount of information that can be stored in an image depends on the number of pixels it contains and the number of possible different intensities or colors that each pixel can have. The actual information content of the image is invariably less than the maximum possible. As well as the uncertainty in the spatial origin of the signal due

to the point spread function, there will be some uncertainty about the reliability of the intensity or color information due to a certain amount of noise in the measured signal.

When we perform image processing we are sorting and manipulating the information in an image. Often we are trying to separate certain parts of the ‘true’ signal from the noise. In doing this we must be careful not to accidentally destroy important information about the imaged subject, and also not to introduce new noise or artifacts that might be accidentally interpreted as information. [2]

I.4.1 Digital image representation:

A digital image is a two-dimensional discrete signal. A digital image is also an $N \times N$ array of elements. Each element in the array is a number which represents the sampled intensity. For example, the representation of a 4 X 4 image in matrix format and its three-dimensional view is shown in Fig. I.4

Converting an image into a digital format can be done either with a digital camera, or by a scanner. Digital images can be created directly on a computer screen. However, it is restricted both in spatial coordinates (sampling) and in its allowed intensities (quantization). [6]

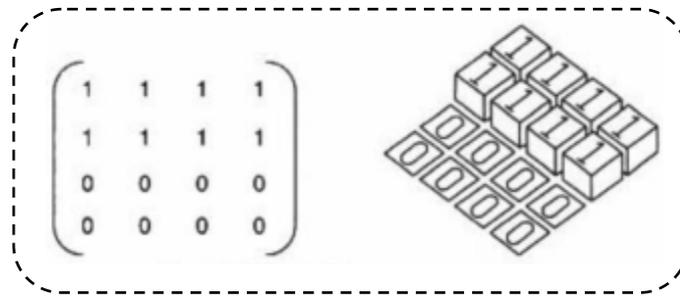


Fig. I.4 Digital image representation [6]

I.4.2 Pixels:

You might say that the fundamental particle of digital imaging is the pixel – the smallest piece of discrete data in a digital image. The pixel represents discrete data, not necessarily discrete information. Due to the point spread function, subject movement, and several other effects, information from the imaged object will to some extent be distributed amongst adjacent pixels (or voxels). When discussing color images we could separate the individual color components of each pixel (e.g. the red, green, and blue data that describe a pixel in an RGB image) but since we are mainly dealing with gray scale images in medical imaging we

need not worry about this refinement here. However, we do have to be careful about the way we use the term ‘pixel’ in digital imaging, even after defining it as a “picture element”. Pixel can mean different things in different contexts and sometimes conflicting contexts are present simultaneously.

A pixel might be variously thought of as:

1. A single physical element of a sensor array. For example, the photosites on a semiconductor X-ray detector array or a digital camera sensor.
2. An element in an image matrix inside a computer. For an $m \times n$ gray scale image there will be one $m \times n$ matrix. For an $m \times n$ RGB color image there will be three $m \times n$ matrices, or one $m \times n \times 3$ matrix.
3. An element in the display on a monitor or data projector. As for the digital color sensor, each pixel of a color monitor display will comprise red, green and blue elements. There is rarely a one-to-one correspondence between the pixels in a digital image and the pixels in the monitor that displays the image. The image data is rescaled by the computer’s graphics card to display the image at a size and resolution that suits the viewer and the monitor hardware. [2]

I.4.3 Volume image:

A three-dimensional image is an example of volume image. The volume image can be obtained from some medical imaging equipment in which the individual data points are called ‘voxels’. Voxels stands for volume pixels. A CAT scan is an example of a volume image. [8]

I.4.4 Image Size, Scale, and Resolution:

Shrinking or enlarging a displayed image is a trivial process for a computer, and the ease of changing the displayed or stored size of images is one of the many advantages of digital imaging over older film and paper based technology. However, technology changes faster than language with the result that terminology, such as references to the size, scale and resolution of an image, can become confused. We may not be able to completely eliminate such confusion, but being aware of the possibility of it should make us communicate more carefully. We may need to be explicit when we refer to these characteristics of an image, and we may need to seek clarification when we encounter images which are described with potentially ambiguous terms.

What is the size of a digital image? Is it the image matrix dimensions, the size of the file used to store the image, or the size of the displayed or printed image? The most common usage defines image size as the rectangular pixel dimensions of the 2D image – for example 512 x 512 might describe a single slice CT image. For very large dimension images, such as digital camera images, it is common to describe the image size as the total number of pixels – 12 megapixels for example.

Image scale is less well-defined than image size. In medical imaging we generally define the Field of View (FOV) and the image matrix size. Together these define the spatial resolution of the raw image data. Many file storage formats include a DPI (dots per inch) specification which is a somewhat arbitrary description of the intended display or print size of the image. Most software ignores the DPI specification when generating the screen display of an image, but may use it when printing. [2]

I.4.5 Image types:

Images can be broadly classified under four categories: Black and white or binary images, grayscale images, color images, and multi spectral images. [9]

I.4.5.1 Binary images:

Binary images take only two values, i.e., either ‘0’ or ‘1’. The brightness graduation cannot be differentiated in the binary image. The binary image representation is illustrated in Fig. I.5

Mother Teresa s image in Fig. I.6 is an example of a black-and- white image. A grayscale image can be converted to a black- and-white or binary image by the thresholding operation. Geometric properties of an object, like the location of the centroid of the object or the orientation of the object, can be easily extracted from a binary image. [6][9]

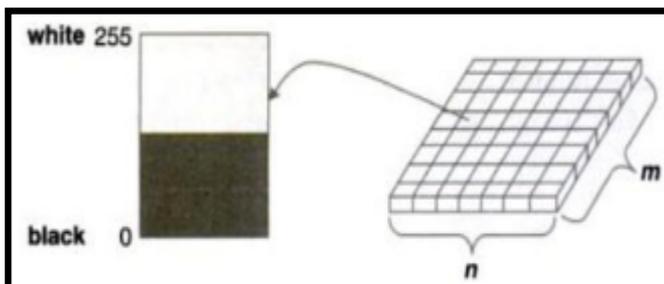


Fig. I.6 Mother Teresa in black and white [6]

Fig. I.5 Binary image representation [6]

I.4.5.2 Grayscale image:

Grayscale images contain only brightness information. Each pixel value in a grayscale image corresponds to an amount or quantity of light. The brightness graduation can be differentiated in a grayscale image. In a grayscale image, each pixel is represented by a byte or word the value of which represents the light intensity at that point in the image. An 8-bit image will have a brightness variation from 0 to 255 where '0' represents black and '255' represents white, as shown in Fig. I.7. A grayscale image measures only the light intensity. Each pixel is a scalar proportional to the brightness. Mother Teresa's image is given as an example of a grayscale image in Fig. I.8. [6] [9]

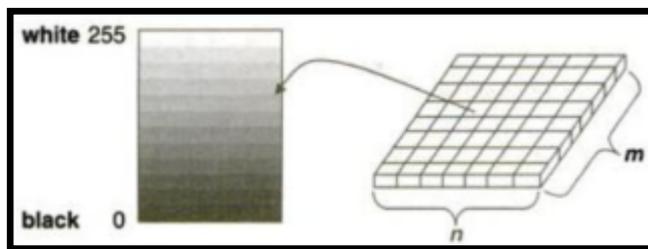


Fig. I.7 Grayscale image representation [6]



Fig. I.8 Mother Teresa in grayscale [6]

I.4.5.3 Color image:

A color image has three values per pixel and they measure the intensity and chrominance of light. Each pixel is a vector of color components. Color images can be modeled as three-band monochrome image data, where each band of data corresponds to a different color. The actual information stored in the digital image data is the brightness information in each spectral band. Common **color spaces** are **RGB** (Red Green and Blue), **HSV** (Hue, Saturation, Value), and **CMYK** (Cyan, Magenta, Yellow; Black). Colors can be represented with three color components as shown in Fig. I.9, so the typical uncompressed data rate of a color image is three times the data rate of a grayscale image. [6]

Kalpana Chawla's image in Fig. I.10 is an example of an RGB image. Color images usually consist of three separate image representations called color planes, with pixel values in each plane corresponding to the intensity of a certain color at a specific point in the image. Each color plane consists of an array of pixel values similar to that of the grayscale representation.

The most popular system is RGB, where three color planes are used to represent the intensity of red green and blue in the scene. [10]

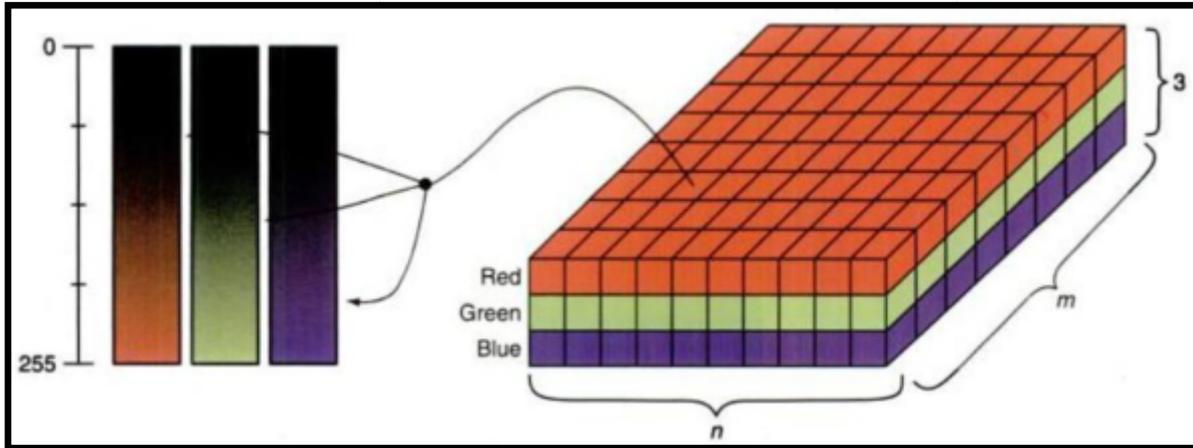


Fig. I.9 RGB image representation [6]

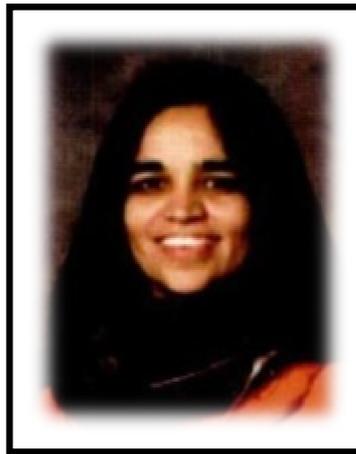


Fig. I.10 Kalpana chawla's colour image [6]

I.4.6 The quality of a digital image:

Any imaging system must be judged on the quality of the images it produces. For medical imaging systems the images must be diagnostically useful, that is capable of leading to the detection and identification of an abnormality and its interpretation so as to determine its cause, and obtained at an acceptable dose to the patient. An image is a spatial pattern of intensities. Fundamentally, the quality of a digital image depends on the size of the pixels, relative to the size of the image, and the number of available values of gray tone that are accessible to describe the intensity range between black and white: image quality is highest for small pixels and a large number of available gray tones. [7]

I.5 Imaging systems:

I.5.1 The human visual system:

The Human Visual System (HVS) is one of the most complex systems in existence. Our visual system allows us to organize and understand the many complex elements in our environment. The visual system consists of an eye that transforms light into neural signals, and the related parts of the brain that process the neural signals and extract necessary information. The human eye serves to project and convert light into neural activity. Light enters the cornea, passes through the aqueous humor, then through the lens into the vitreous humor, and finally onto the photoreceptors located at the back of the retina. The ciliary muscles are responsible for accommodating the lens so as to focus the light rays onto the fovea, the region of the retina containing the greatest density of cones, and thus the high acuity for spatial and color vision. [6]

I.5.2 Anatomy of the human visual pathway:

In order to design efficient image processing systems it is important to have an understanding of the human visual pathway, which comprises the eye, its associated nerves and portions of the brain.

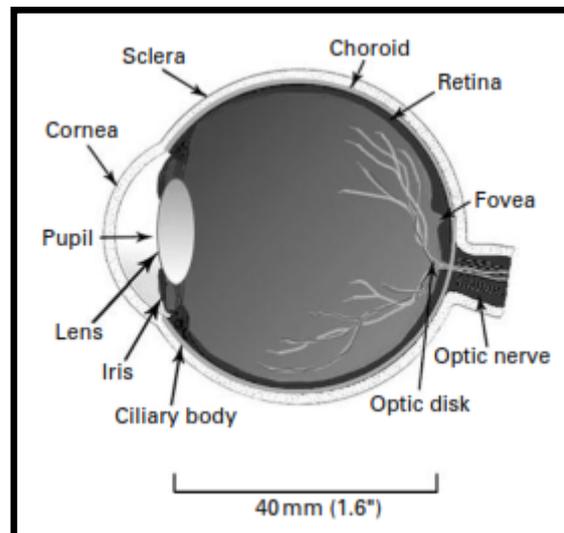


Fig. I.11 Cross-section through a typical human eye [7]

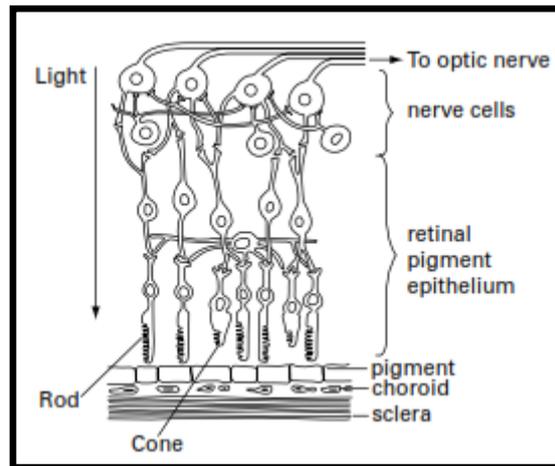


Fig. I.12 Structure of the photoreceptors of the human eye [7]

The eye is almost spherical in shape, with an average diameter of about 40mm (Fig. I.11). It converts information entering through the pupil as visible light into electrical impulses, which are transmitted along the optic nerve to the brain, for interpretation. Visible light is refracted by the cornea and enters the pupil, after which it is again refracted, by the lens, to form an inverted image on the innermost membrane of the eye, the retina. The retina is composed of several layers, and one of these, the retinal pigment epithelium, contains the photoreceptors that sense the light and convert it to electrical impulses which are taken by the optic nerve to the brain. There are two types of photoreceptor, rods and cones (Fig. I.12). The rods are more numerous, with about 100 million distributed throughout the entire layer; they are more sensitive to light than the cones. There are fewer cones, about 6–7 million, and they are highly concentrated, approximately 180000 mm^{-2} , in a circular region near the center of the retina, about 1.5 mm in diameter: the fovea.

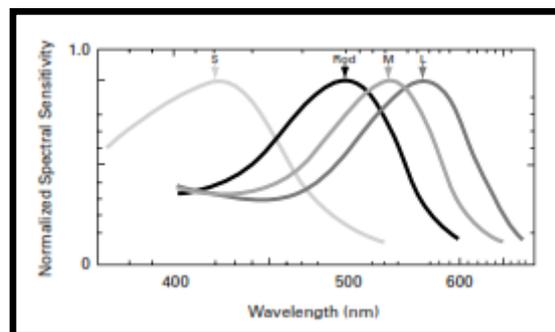


Fig. I.13 Spectral sensitivity of the rods and cones. (Note that each curve has been normalized to the same peak height.) [7]

Complicated cross-linking of cells facilitates some basic processing even before the information leaves the retina. There is a region, devoid of photoreceptors, where the optic nerve leaves the retina: it is known as the optic disk and accounts for the blind spot in the visual field. Rods are sensitive to blue-green light, with peak sensitivity at a wavelength of around 498nm, but they cannot detect color, only light intensity. Several rods are connected to a single nerve, and this makes them unable to discern fine detail. They can function in situations of low light intensity and are vital for night vision. There are three types of cones, which together permit color vision: their sensitivity overlaps with L-cones (red or Long-wavelength), having peak sensitivity around 564nm, M-cones (green or Medium wavelength), with peak sensitivity around 533nm, and S-cones (blue or Short wavelength), with peak sensitivity around 437nm (Fig. I.13). [7]

I.6 Image storage:

The storage and transmission of medical images is obviously of critical importance to medicine. Images must be stored safely to protect both the integrity of the data and the privacy of patients, but images also need to be easily available when and where they are needed by medical staff. The imaging software user will normally have the option to store processed images in a number of different standard formats. Although the methods of transmission of images are generally not of concern to image acquisition and processing it is important to be aware that the time required for transmission depends on the size of the image file. [2]

I.6.1 Image file format:

The choice of image file format has implications for:

1. The size of the stored image file
2. The type and amount of metadata that can be stored
3. The availability of multiple layers and transparent layers
4. The flexibility or 'customizability' of the content
5. The integrity of the data
6. The speed of image transmission
7. Software compatibility

All general-purpose file formats are designed to handle color images. The medicine specific formats, e.g. **DICOM**, are primarily designed for gray scale images but are flexible

enough to store color images when necessary. The following is a simplified overview of some common image file formats. Most of these formats utilize or enable image data compression. Like: bitmaps and BMP files, JFIF (JPG) (JPEG File Interchange Format), GIF (The Graphic Interchange Format), PNG (The Portable Network Graphics), TIF or TIFF (The Tagged Image File Format), **DICOM** (Digital Imaging and Communications in Medicine).

Image data compression methods are categorized as either lossless (no intensity or color information is lost in compression), or lossy (some intensity or color information is lost). Section 1.6.3 below discusses compression methods in more detail. [2]

I.6.2 What is DICOM?

You can walk with this question into most modern, digital, state-of-the-art hospitals and spend hours looking for someone who could answer it correctly. We all get used to buzz words and acronyms, and rarely think about their meanings. Unfortunately, nothing distances you more from success than not knowing what you are dealing with! DICOM stands for *Digital Imaging and Communications in Medicine* and represents Years of effort to create the most universal and fundamental standard in digital medical imaging. As such, it provides all the necessary tools for diagnostically accurate representation and processing of medical imaging data. Moreover, Contrary to popular belief, DICOM *is not just an image or file format*. It is an all-encompassing data transfer, storage and display protocol built and designed to cover all functional aspects of contemporary medicine (which Is why many view DICOM as a *set* of standards, rather than a single standard). Without a doubt, DICOM truly governs practical digital medicine. [11]

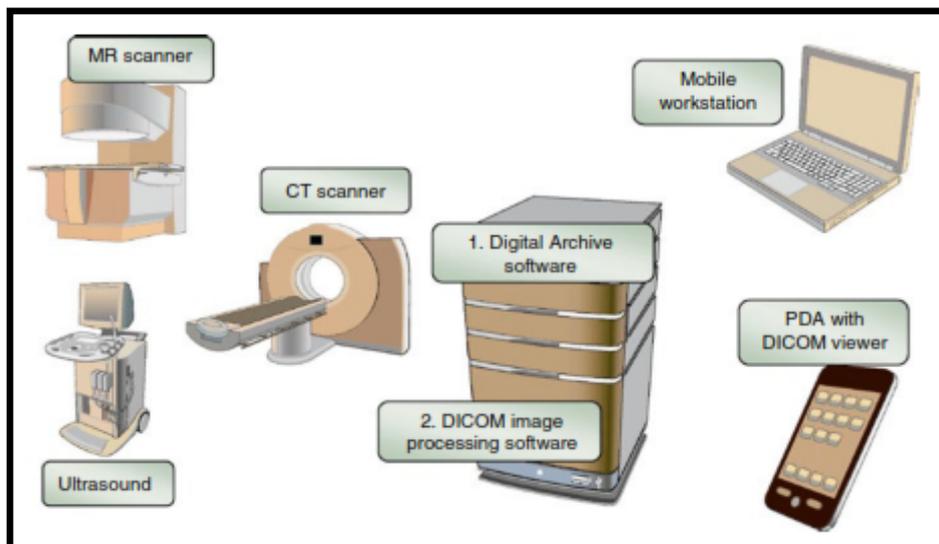


Fig.I .14 DICOM Application Entities. [11]

- Note that Application Entities can be programs, so multiple AEs can be running on the same device, as shown for the archive server

I.6.3 Image Data Compression Methods:

Many image file storage formats compress the image data to reduce storage space requirements and speed image transmission. Most image processing software permits the user to specify whether or not to compress the data and what compression method to use. As mentioned above, the choice of method may be based on software compatibility but also on whether any loss of information can be tolerated. Lossy data compression methods discard the information that is considered to be least obvious to human perception and can often achieve an 80–90% reduction in file size.

Lossless compression methods reduce the size of the stored data by methods that are perfectly reversible – they eliminate only redundant data. Images stored with lossless compression methods are identical in information content to their uncompressed counterparts.

Three different kinds of redundancy are possible in image data:

1. **Coding redundancy.** This is the type of redundancy described above where the data encoding method has more precision than is necessary for a particular image. This type of redundancy can be addressed by using a reduced bit depth and a lookup table.
2. **Spatial redundancy.** This occurs when there are large regions of identical pixels each containing identical information – for example the black background of an X-ray image. This redundancy can be reduced by a method that encodes the description of homogeneous regions.
3. **Information redundancy.** This is information that cannot be perceived – for example spatially small regions with very small differences in intensity and color cannot be seen by humans. This redundancy can be eliminated by making such regions homogeneous. Note that such newly homogenous regions will then be amenable to elimination of spatial and coding redundancy.

Image data compression methods take advantage of the spatial, intensity, and information redundancy just described. Statistical analysis of the image data can lead to further improvements in compression. If we make the assumption that the least common pixel intensities do not represent significant image information then we can omit them from the lookup table by changing them to the closest more common value. Similarly, we might decide

that single pixel, or small groups of pixels that do not fit some measured pattern or trend found in their neighborhood are not important and replace their original values in the stored encoding. The more assumptions of this kind we make the more space we save, but more original image information is lost.

Some of the most popular data compression methods:

- **JPEG:** The JPEG compression algorithm includes both lossless and lossy steps. A modified method, **JPEG2000**, has been developed to address some of the deficiencies of the original JPEG method. It is not yet in common usage and cannot be decoded by most image display and processing software, however, it is supported by the **DICOM** standard.
- **Packbits:** Packbits is a lossless compression method that uses run length encoding (RLE).
- **ZIP, PKZIP:** ZIP (derived from PKZIP) is a general purpose lossless data compression method. It can be used within an image file format (e.g. TIFF)
- **LZW:** LZW (Lempel-Ziv-Welch) is a lossless compression method used in GIF images and is available in some TIFF implementations. [2] [12]

I.6.4 Which method is best?

We have looked at some of the most common file formats and image data compression methods. **Fig. I.15** compares the file sizes and image quality for several of these. There are a few important points to notice: (1) in the absence of compression there is little differences in file sizes. (2) Both the type of image data and the compression method have a major effect on the compressibility. (3) The lossy JPEG method does not always provide greater compression than lossless methods. (4) Lossy methods do not always produce visible degradation of image quality. [2]

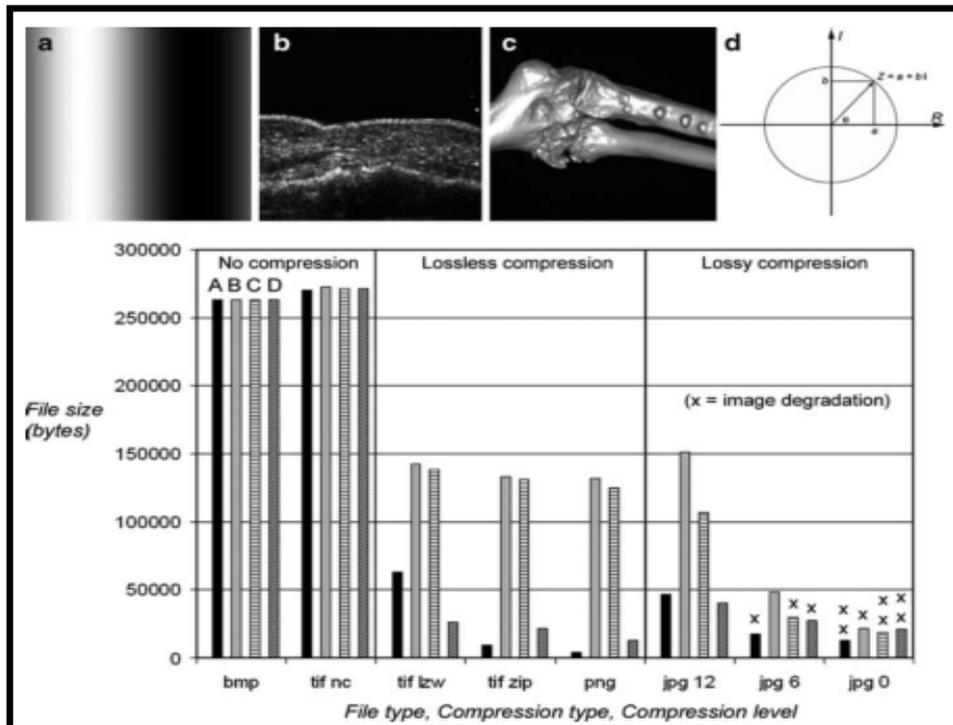


Fig. I.15 Comparison of file sizes for different image types, file types, and compression methods. The ‘compressibility’ of an image depends on its content and the compression method. In the case of lossy compression the severity of image degradation depends on both the degree of compression and the image content. Points to note: Lossless PNG compression outperforms even the lossiest JPEG compression for images (a) and (d). The ultrasound image (b) is only slightly degraded even at the highest level of JPEG compression (All original images were 512 _ 512 pixels, bit depth 8, gray scale. The compressed images are not shown.) [2]

I.7 Conclusion:

We have seen in this chapter a few of the features of a good introductory of digital image and its principles, such as image information, digitizing an image and the quality... etc. In conclusion, digital image analysis provides objective information thus; it can be useful in medical imaging with diagnosing of tumors.

The principle of medical imaging concerns the next chapter.

CHAPTER II

Fundamentals of medical imaging

II.1 Introduction:

Most of the attributes of digital images and the methods of image processing introduced in this text originate from outside of medicine. We can single out medical imaging for special consideration because the lives of people often depend on correct acquisition, processing, and interpretation of medical images. It is important that individuals responsible for acquiring and processing medical images understand both the nature of the raw material they work with, and the way the images they produce will be used. Those using medical images for research, rather than purely clinical purposes, also need to understand the way their raw data is acquired to ensure the scientific rigor of their work.

The purpose of medical imaging is to reveal and record the structural or functional state of the body. Mostly we want to see what is going on inside the body – to check that all is well, or to find out why all is not well. Sometimes we want a record of the current state of the body to be referred to at some future time – to monitor the progress, or absence of progress, of a disease or a treatment. [2]

II.2 Medical imaging modalities:

Medical imaging systems detect different physical signals arising from a patient and produce images. An imaging modality is an imaging system which uses a particular technique. Some of these modalities use ionizing radiation, radiation with sufficient energy to ionize atoms and molecules within the body, and others use non-ionizing radiation. Ionizing radiation in medical imaging comprises x-rays and γ -rays, both of which need to be used prudently to avoid causing serious damage to the body and to its genetic material. Non-ionizing radiation, on the other hand, does not have the potential to damage the body directly and the risks associated with its use are considered to be very low. Examples of such radiation are ultrasound, i.e. high-frequency sound, and radio frequency waves.

The modalities which use ionizing radiation, and the issues involved, have been grouped in this chapter, while the modalities which use non-ionizing radiation are dealt also in this chapter. Our treatment of the imaging modalities is not exhaustive, and concentrates on the images and the issues encountered in obtaining them rather than the technical details of the imaging equipment. [7]

II.2.1 Medical images obtained with ionizing radiation (X-rays imaging):

X-ray imaging obtained with ionizing radiation, it has been used in clinical diagnosis almost from the time of Roentgen's discovery of x-rays. X-rays are generated in an x-ray tube, which consists of an evacuated tube with a cathode and an anode (Fig. II.1(i)). Heating a tungsten filament within the cathode releases electrons by thermal excitation. The filament is located within a depression or cup having sharp contoured edges which electro statically focus the electron beam (Fig. II.1(ii)). Increasingly negative voltages applied to the cathode cup can focus the electrons into a narrow beam or even switch off the beam entirely. The electrons are accelerated towards the positive (50–120 kV) anode, where they strike an embedded tungsten target, producing x-rays. The tube is evacuated so that the electrons pass to the anode in a straight path, and are not scattered by other particles in the tube. The majority of x-ray tubes, apart from those in low output dental and small mobile x-ray units, employ rotating anodes so that the electrons strike a larger area around the rim of the anode and do not over-heat the target. The region on the target from which x-rays are produced is called the focal spot, and its diameter is known as the focal spot size.

The electrons acquire a large kinetic energy during their acceleration in the electric field. When an electron is accelerated through an electric potential of 60 kV, for example, it acquires an energy of 60 keV, where the electron-volt (eV) is a small unit of energy ($1 \text{ eV} = 1.6 \times 10^{-19} \text{ J}$). The electrons lose this energy when they are decelerated at the target. About 99% of the energy lost by the electrons goes into heat and the remaining 1% is converted into x-rays. [13]

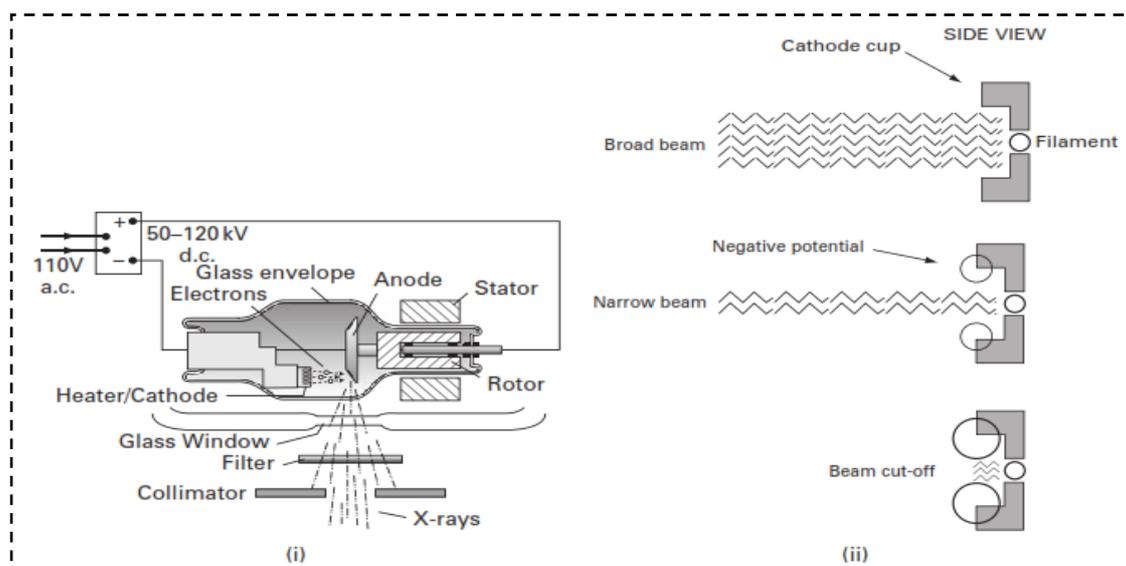


Fig. II.1 (i) A standard x-ray tube; (ii) focusing the electron beam using a negative voltage to the cathode cup. [7][13]

II.2.1.1 X-ray radiography: The first revolution

Diagnostic medical imaging started just over 100 years ago with the discovery of X-rays by Roentgen in 1896. Within a year of his announcement, \$16 home X-ray sets could be bought in the US and a Birmingham doctor in England performed the first X-ray guided operation to extract a fragment of a sewing needle embedded in the hand of a seamstress. Specialised X-ray diagnostic and therapeutic methods developed throughout the century and, up until about 1960, X-ray methods completely dominated non-invasive medical diagnosis. Even today the various specialised modifications of simple projection X-ray radiography are by far the most frequently used diagnostic techniques in medicine. In some areas, such as mammography, X-rays provide the gold standard for the early detection of breast cancer. Dentistry relies almost entirely on X-rays. [3]

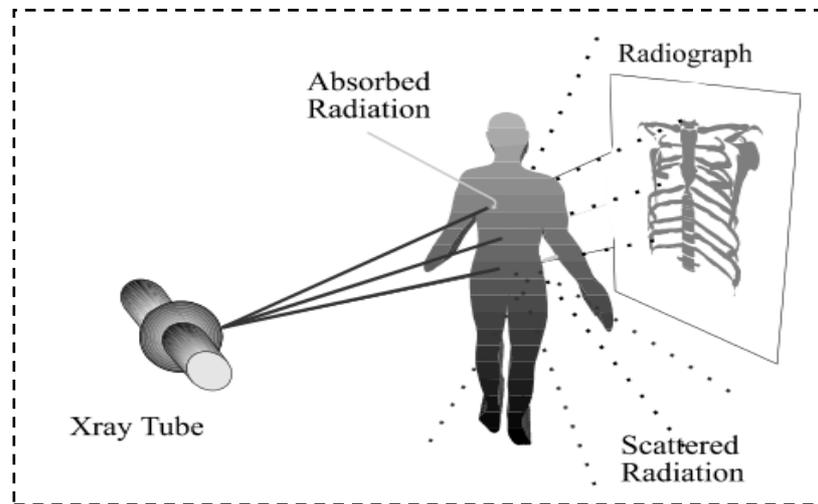


Fig. II.2 A typical X-ray radiographic geometry. X-ray photons generated by the tube are directed at the patient. A fraction of the photons pass directly through the body to create a 2-dimensional projection of the exposed anatomy. [14]

X-ray detectors used in medical imaging consist of an x-ray attenuator that transduces the x-ray signal into either an optical signal (typically by a phosphor) or an electronic signal (typically by a semiconductor), and a device for recording the light or electrons. While historically the optical signal (light) was recorded by film, this has largely fallen out of practice. Today, two broad classes of digital detectors are most commonly used; these go by the rather confusing names of computed radiography (CR) and digital radiography (DR).

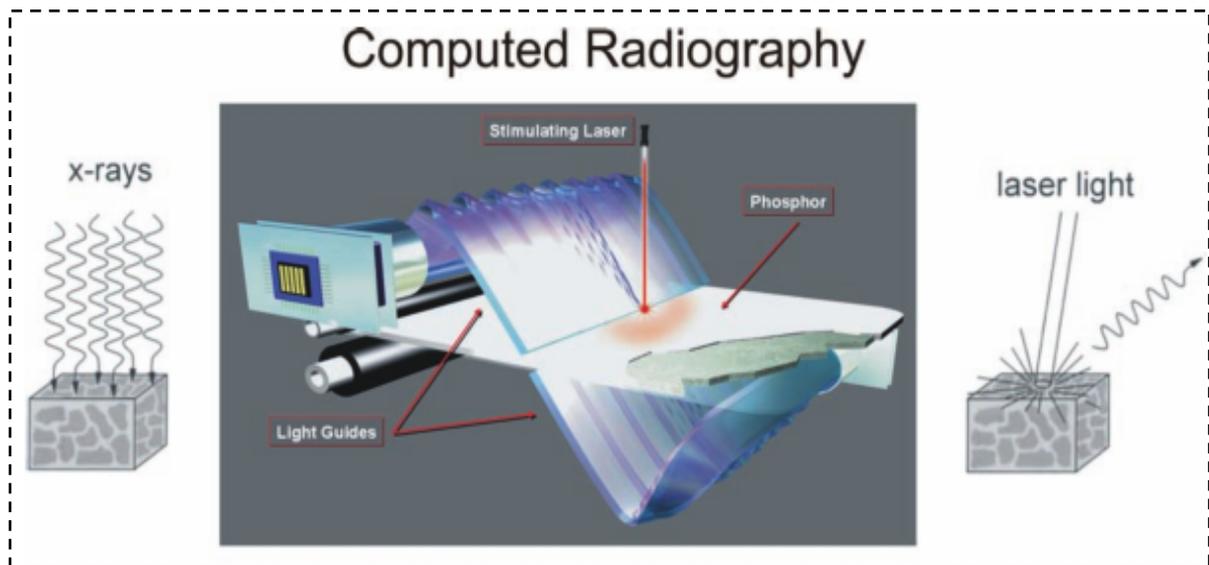


Fig. II.3 Computed radiography detectors. In (CR), x-rays excite a phosphor which traps the liberated charge (left). The phosphor plate is then raster-scanned by translating a plate past a scanning laser. The laser stimulates the emission of light (right). The stimulated light is collected by light guides and recorded to produce the radiograph. [15]

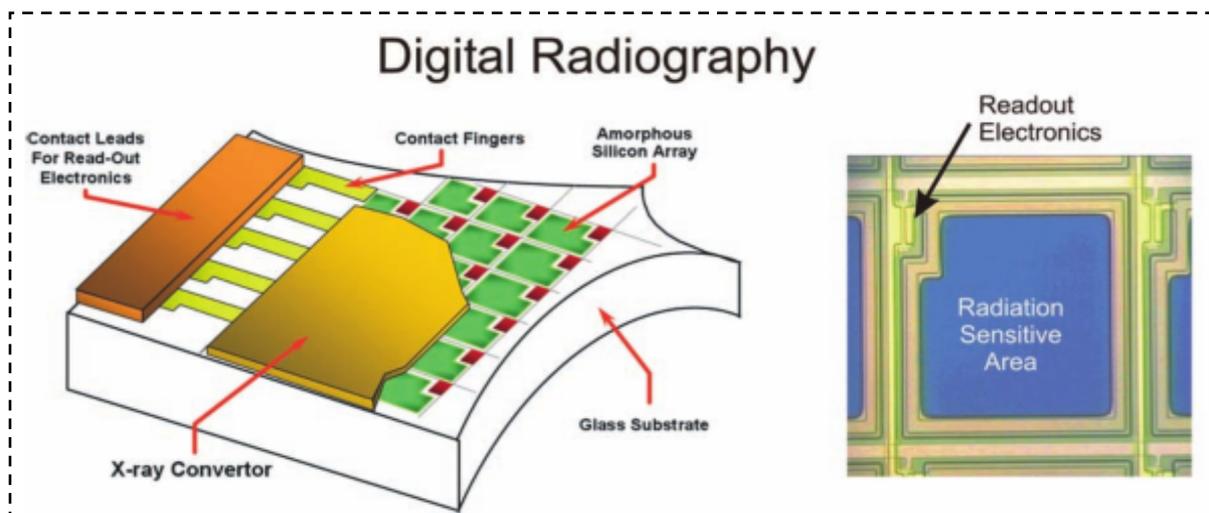


Fig. II.4 Digital radiography image detectors. In (DR), a flat-panel detector consists of an array of photo detectors coupled to an x-ray converter (bottom left). Each photo detector consists of a radiation-sensitive area and readout electronics made up of thin-film transistors. The array of detector elements is read in a raster fashion to produce an image. [15]

At the current time, CR systems are used exclusively for radiography. DR systems can be used for both radiography and fluoroscopy. [15]

➤ Images from radiography:



Fig. II.5 Posterior–anterior chest radiographs of (i) a normal patient and (ii) a patient suffering from tuberculosis. [7]

II.2.1.2 X-ray fluoroscopy:

Fluoroscopy is radiography's first cousin, the clever one that lets the physician watch continuously changing processes live in real time as they take place, rather than as one or a few radiographic snapshots developed later. To achieve this, it employs a more complex image receptor.

The X-rays that pass through and emerge from the patient do not expose a film cassette but rather, in most fluoro systems, they project directly onto the front face of an *image intensifier* (II) tube. An II is an electronic vacuum tube device that can transform a life-sized, very faint pattern of X-ray energy into a small, bright corresponding pattern of visible light. The output of the II tube used to be photographed directly with a still or cine film camera or viewed with a TV camera. These days, a solid state electronic *charge-coupled device* (CCD) or a *complementary metal oxide semiconductor* (CMOS) optical camera does the job.

- ✓ fluoroscopy = X-ray tube + image intensifier tube + solid-state CCD or CMOS electronic optical camera: (figure. II.6).

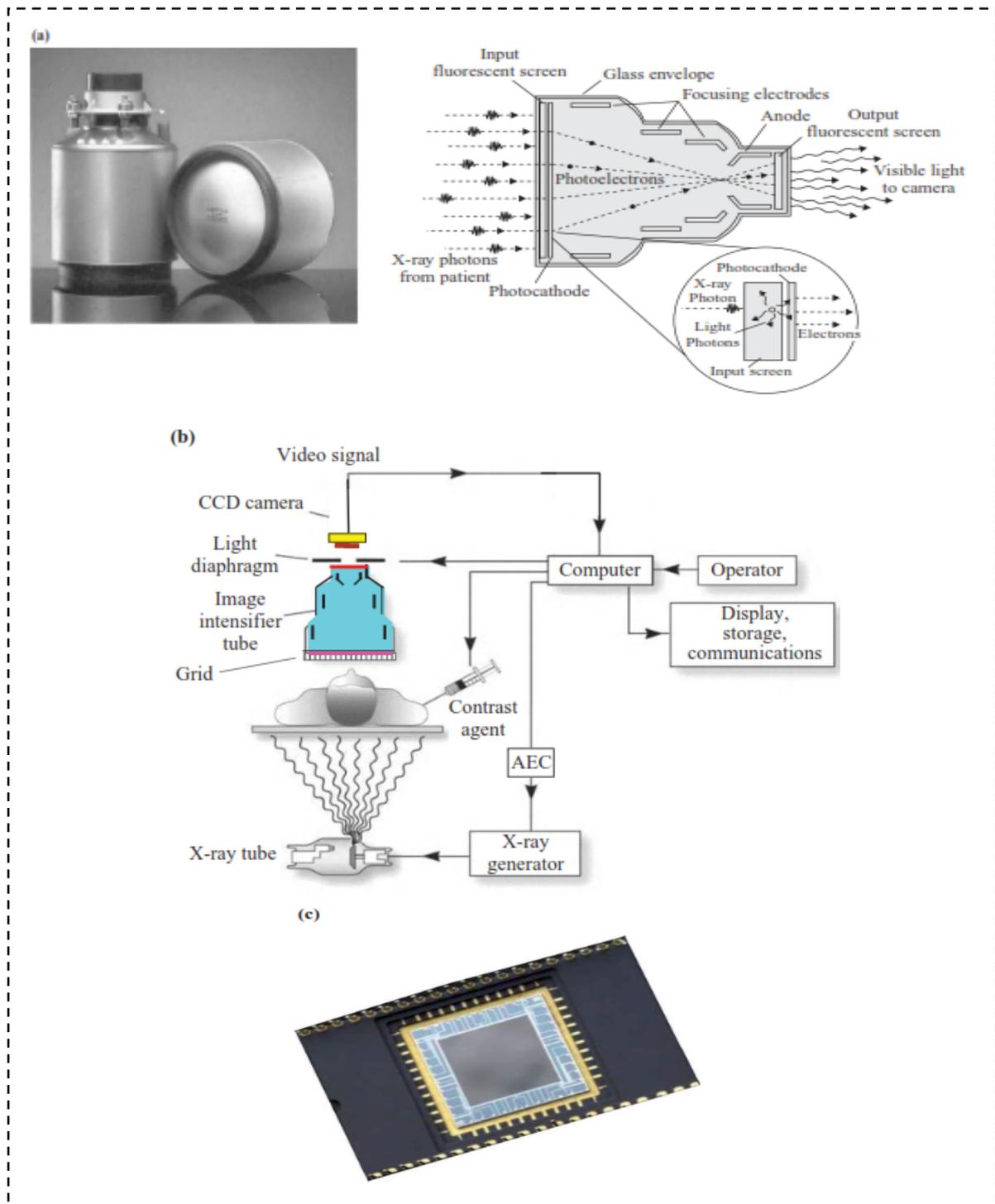


Fig. II.6 Modern fluoroscopy. (a) An image intensifier (II) is an electronic vacuum tube that transforms the life-sized X-ray shadow pattern emerging from a patient into a small, very bright optical image ready to be viewed by an electronic optical camera and fed into a computer. (b) Block diagram of a modern II-based fluoroscopic system, where everything is under computer control. (c) A small solid state electronic optical camera, such as a charge-coupled device (CCD) that observes the output of the II tube and sends its signal to the computer. [16][17]

➤ **Images from fluoroscopy:**

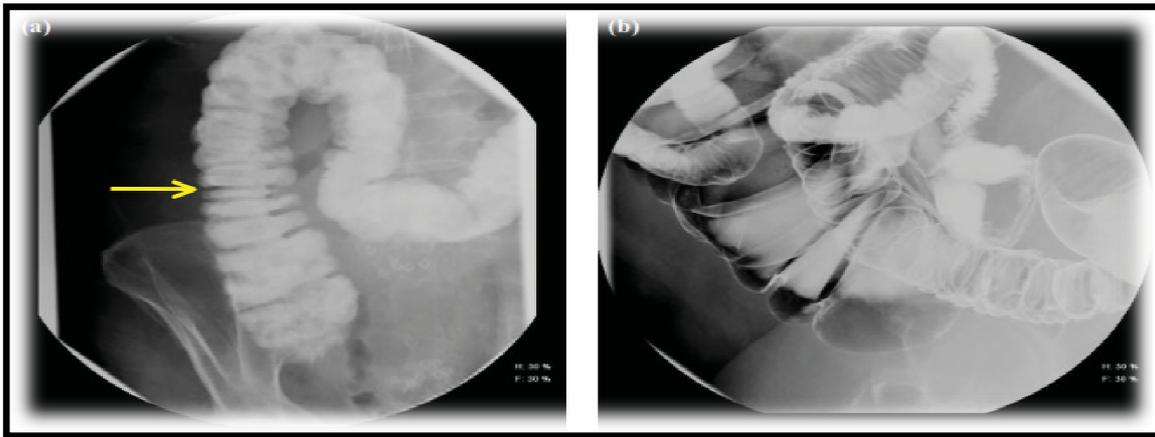


Fig. II.7 Fluoroscopic examination of the GI tract with contrast agent. (a) In a barium enema study. (b) A radiolucent material such as insufflated air can then be introduced to fill the lumen of the colon. [17]

II.2.1.3 X-ray CT: The second revolution

X-ray CT on its own has been a remarkably successful innovation in medicine. Even medium sized hospitals routinely use CT for the rapid assessment of structural abnormality resulting from injury or disease throughout the body. CT has also become a standard tool in the planning of cancer radiation treatment. The CT image often provides a clear definition of the extent of the tumor and its disposition with respect to surrounding healthy tissue. The intrinsically digital format of CT allows the radiologist to calculate optimum paths for the therapy beams to deliver a lethal dose to the cancer but spare healthy tissue. CT has some important drawbacks: it entails a relatively large dose of ionising radiation to the patient and there are practical limits on spatial resolution brought about by the very small differences in X-ray contrast between different types of soft tissue. The medical success of CT, together with these limitations, spurred the development and hastened the introduction of MRI into regular hospital use in the early 1980's.

CT scanners consist of an x-ray tube and an opposing x-ray detector mounted on a circular ring. In most CT scanners, the x-ray generator and data processing system are also mounted on the ring. These elements rotate about the patient to acquire projections through the patient at various angles. The rotating ring is most commonly arranged in a vertical plane,

while the patient is prone or supine on a horizontal bed. The bed is advanced through the center of the ring as the acquisition system is rotated about the patient (Fig. II.8).

The x-ray tube and generator for CT are designed to allow substantially longer exposure times than conventional radiographic systems. [15]

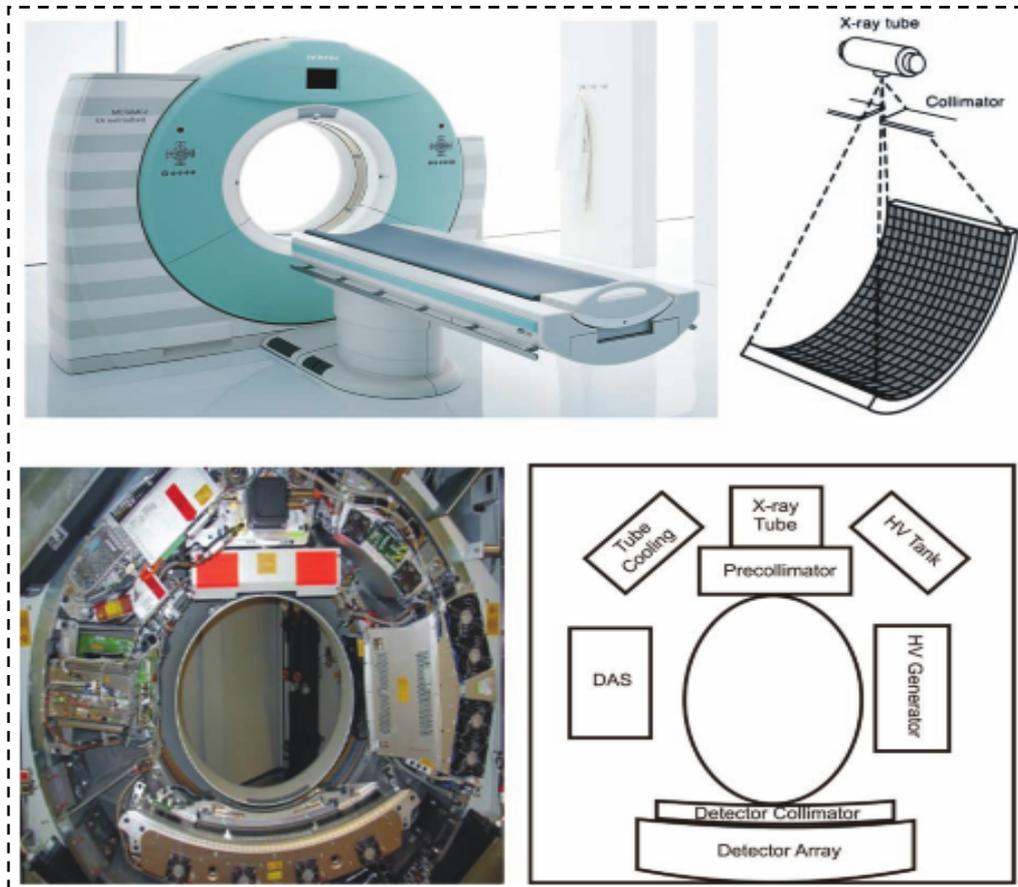


Fig. II.8 A modern CT scanner. [15]

CT scanners have been evolving continuously since the early 1970s. A few of the changes, however, have been sufficiently radical to distinguish what are known currently as the seven generations of CT devices, where the last two incorporate helical motion and multi-slice capability. New machines are nearly all of the helical, multi-slice variety (Fig. II.9). [15]

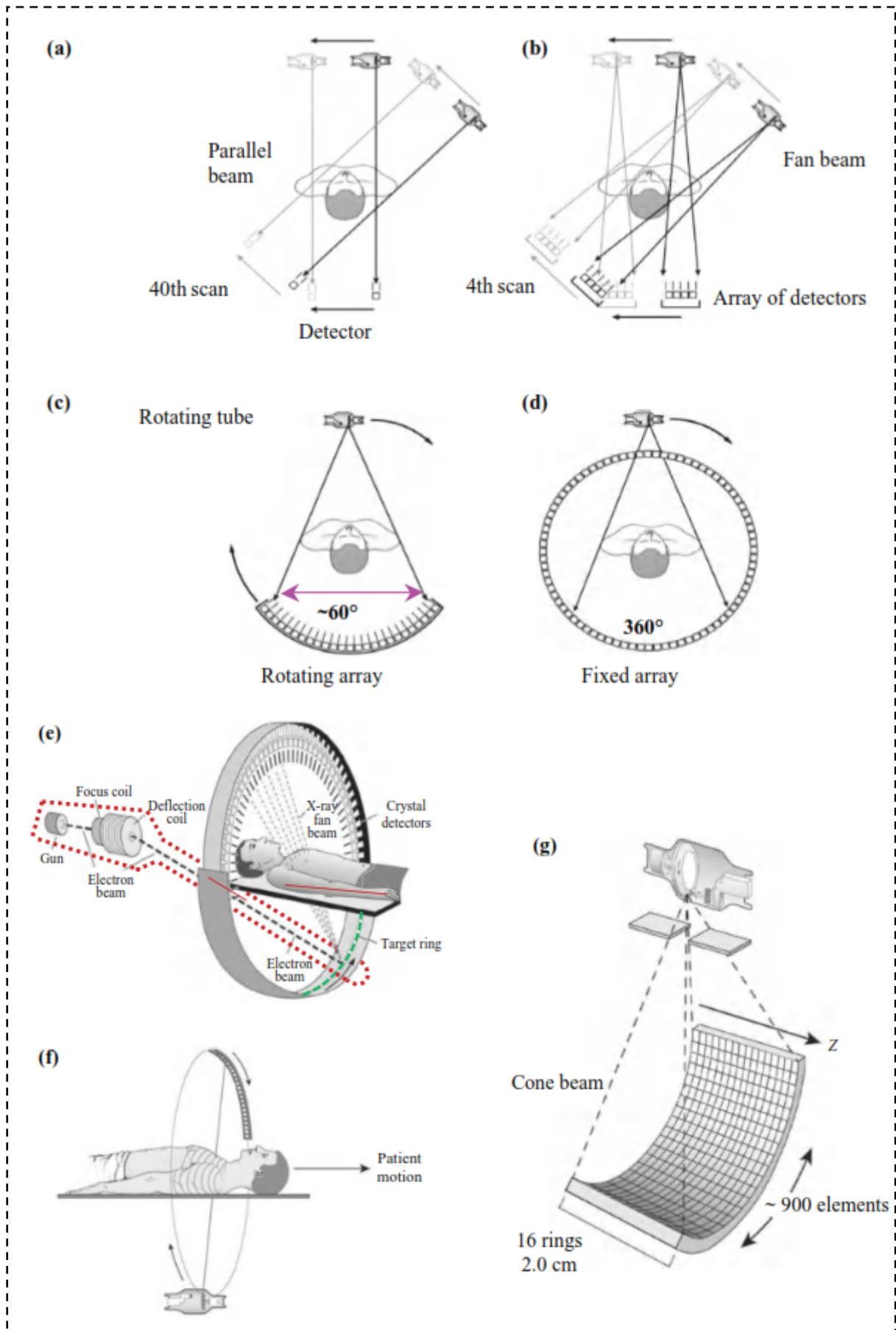


Fig. II.9 The seven generations of CT scanners

Where: (a) First generation: the original EMI head scanner: translate, then rotate the linked tube/pencil beam and the detector, and repeat 180 times. (b) Second generation: translate-rotate with a fan-beam and bank of detectors; much faster; the fan is 10 (rather than 1) degrees wide, so only 1/10 as many scan angles are needed. (c) Third generation: rotating tube and rotating $\sim 60^\circ$ -detector assembly. (d) Fourth generation: rotating tube and fixed 360° ring of detectors. (e) Fifth generation: electron-beam tomography CT, great while it dominated, but driven nearly extinct by seventh-generation devices. (f) Sixth generation: helical/spiral, in which the table moves smoothly forward as the gantry rotates continuously; made possible by slip-ring technology. (g) Seventh generation: helical multi-slice CT typically obtains 64 slices (but currently up to 320) with each rotation of the gantry. Built upon third-generation design and used in either sequential/axial or helical/spiral mode. [15]

➤ Images from CT:



Fig. II.10 Contrast enhanced CT images in intersecting coronal and axial planes show the mass located at the level of the right adrenal gland, representing a pheochromocytoma (arrows). [18]

II.2.1.4 X-ray mammography:

X-ray mammography is one of the most challenging areas in medical imaging. It is used to distinguish subtle differences in tissue type and detect very small objects, while minimizing the absorbed dose to the breast. Since the various tissues comprising the breast are radiologically similar, the dynamic range of mammograms is low. [7]

Mammography is a form of radiography specialized and refined specifically for imaging the breast. One is normally searching for lesions that are small and very similar radiologically to the surrounding breast soft tissues, and also for microcalcifications. Both excellent contrast and exquisite resolution are essential, and that requires a radiation exposure high enough to achieve an acceptable signal-to-noise ratio. At the same time, the breast is sensitive to ionizing radiation, so it is also critical to keep dose as low as reasonably achievable for reasons of safety.

Achieving an optimal balance between creating clinically adequate images, while at the same time keeping the risks “acceptably” low, is difficult with all forms of imaging with ionizing radiation, but it is especially so for the breast. None of contrast, resolution, noise, and dose objectives is particularly easy to achieve separately, and producing a single imaging device that can satisfy them all simultaneously has required heroic design ingenuity (Figures II.11a and b). First to achieve this was screen-film mammography, with low-energy molybdenum (Mo) characteristic X-rays (rather than bremsstrahlung) generated by a special tube with particularly small focal spots on a Moly target and detected with special mammography film, with emulsion on one side only for better resolution, within a single-screen cassette (Figure II.11c).

The utility of a mammogram depends, ultimately, on its ability to allow the clinician to discriminate among the various normal and abnormal breast tissues. The attenuation properties of glandular, adipose, muscle, skin tissues, and neoplasms are alike, and often differences are not visible with standard projection radiography.

In film mammography, single-emulsion film, without an intensifier screen, is used to minimize the detector contribution to unsharpness, even though this necessitates the use of higher x-ray doses: in digital mammography, the film is replaced by semiconductor sensors. [17]

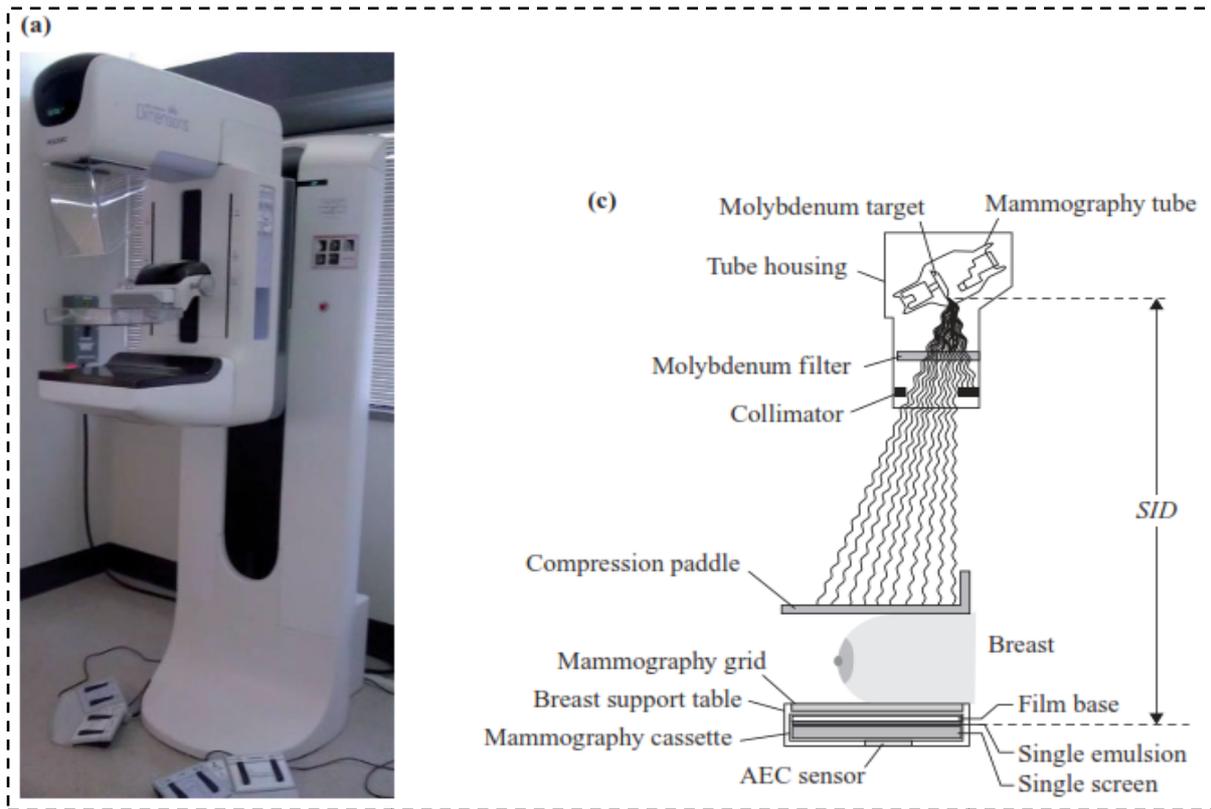


Fig. II.11 Mammographic imaging. (a) A modern mammography unit. (b) Mammographic stereotactic needle biopsy system for patient in the prone position. [17]

➤ **Images from mammography:**

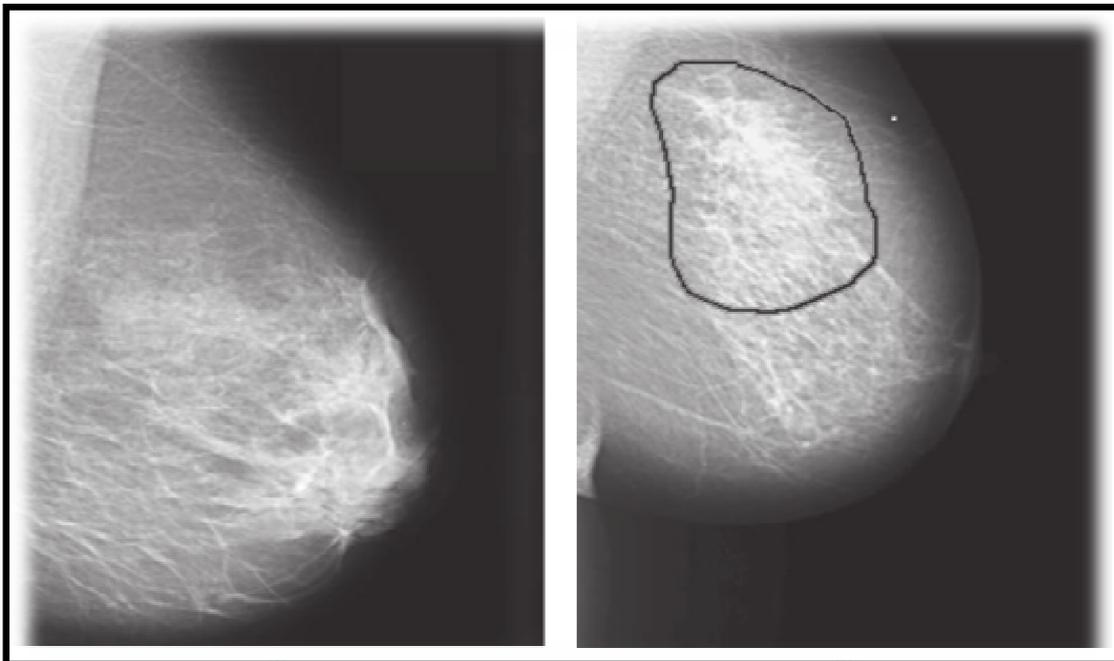


Fig. II.12 (i) Normal breast. (ii) Dense opacity and spiculations (in the outlined area) indicative of a malignant lesion. [7][19]

II.2.2 Medical images obtained with non-ionizing radiation:

Diagnostic medical ultrasound uses high-frequency sound and a simple pulse-echo technique. When an ultrasound beam is swept across a volume of interest, a cross sectional image can be formed from a mapping of echo intensities. Current medical ultrasound imaging systems are based on envelope detection, and therefore only display intensity information. Despite this shortcoming, ultrasound imaging has become an important and widely accepted modality for non-invasive imaging of the human body because of its ability to produce real-time images, its low cost and its low risk to the patient. Magnetic resonance imaging (MRI) uses the phenomenon of nuclear magnetic resonance (NMR): unpaired nucleons, such as protons, orientate themselves in a magnetic field, and radiofrequency pulses can be used to change the balance of the orientations. When the system returns to equilibrium it produces signals that can be used to produce an image, which is characterized by its high contrast for soft tissues. MRI images map function, as well as structure. Digital images from any imaging modality can be compared or combined, after image registration, using a networking system. [7]

II.2.2.1 Ultrasound imaging (US):

Although ultrasonic waves could be produced in the 1930's and were investigated as a means of medical imaging, ultrasound imaging did not start properly until after World War 2. It benefited from the experience gained with SONAR, in particular, and fast electronic pulse generation in general. The first two-dimensional image, obtained using sector scanning, was published in 1952 by Wild and Reid. Application to foetal imaging began in 1961 shortly after the introduction of the first commercial two dimensional imaging systems. Today, ultrasound imaging is second only to the use of X-rays in its frequency of clinical use. [3]

Ultrasound (US) consists of high-frequency sound waves that are above the range of human hearing, at frequencies higher than 20 kHz. Medical ultrasound imaging is performed at much higher frequencies, typically in the MHz range. Ultrasound differs from other conventional imaging methods in important ways. First, unlike electromagnetic radiation, ultrasound waves are non-ionizing pressure waves. Second, the ultrasound signal is recorded in the reflection mode rather than the transmission mode used for x-ray and CT imaging. In ultrasound imaging, the imaged structures are not the sources that emit radiation. Instead, the sample is imaged by applying external acoustic energy to it. A "pulse echo" technique is used

to create an image from longitudinal mechanical waves that interact with tissues of the body. The applied energy is reflected to the source by tissue inhomogeneities. The resulting signals carry information about their source as well as about the sample. Decoding these signals into an image requires separating the detected signal components due to the external source from those due to the sample. [15]

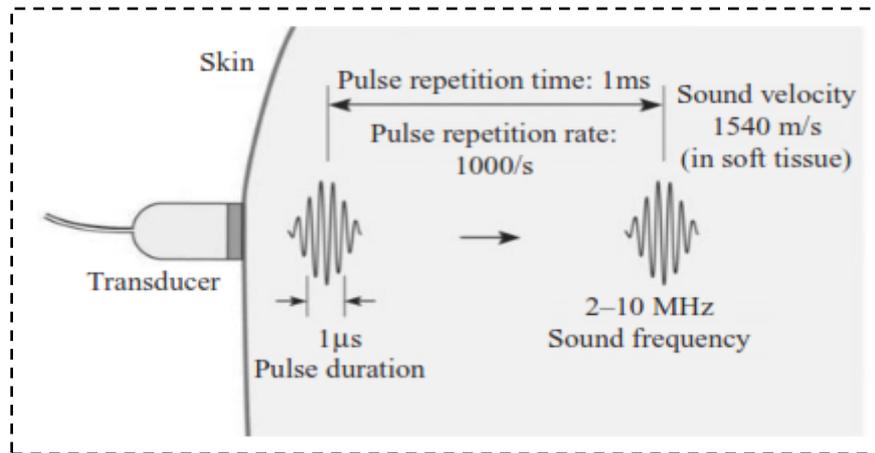


Fig. II.13 A typical US beam consists of 2- to 10-MHz pulses that are 1 microsecond (μs) short and repeated every 1 millisecond (ms). In soft tissue, ultrasound pulses travel at about $1540\ \text{m/s}$, with very little dependence on their frequency. [7][17]

The heart of a US system is the transducer, an energy conversion device that transforms pulses of electrical voltage into mechanical vibrations, and vice versa. The transducer is pressed against the body and, acting somewhat as an audio speaker, produces a narrow, focused beam of pulses of US. In a homogeneous material, such as water or the fluid contents of a cyst, the beam simply dissipates its energy as it penetrates to greater depths, somewhat analogous to the attenuation of a monochromatic beam of X-rays passing through a homogeneous medium. But if a beam passes from one tissue into another, energy is also reflected back at the interface between them (Figure II.14a).

By analogy, imagine a pair of joined springs of different mass per length or elasticity (Figure II.14b). When a pulse moving along from one end encounters the junction, some of its energy will continue in the forward direction but the rest will be reflected back as an echo; in an extreme case, with the spring attached to a wall, virtually the entire pulse will be reflected, but returned upside-down. This figure is a little misleading, however, in that the displacements of the spring are shown as transverse to the direction of wave propagation; with

sound and ultrasound, they are longitudinal, vibrating back and forth along the direction the waves are moving.

After reflection at inter-tissue boundaries, the US echoes are detected by the transducer, now serving as a microphone, and transformed back into electrical signals. The time of return of an echo is proportional to the depth within the patient of the interface that produced it. The echo's intensity depends on the degree of difference in density and/or elasticity of the materials on the two sides of the interface, as well as on its depth. [17]

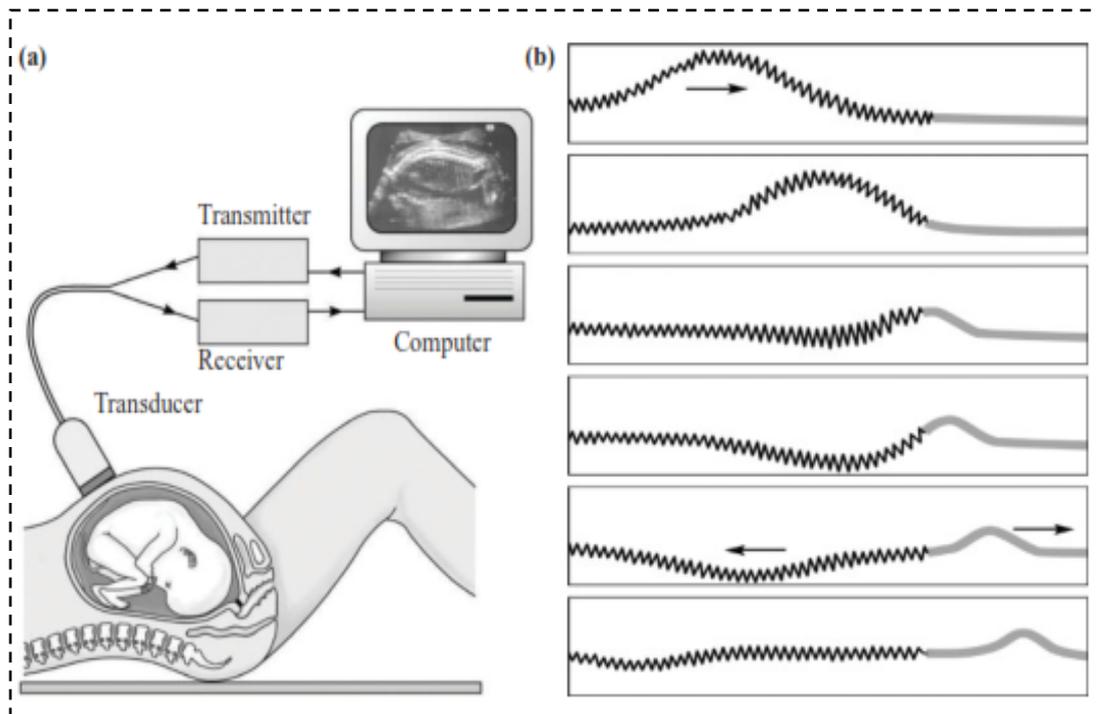


Fig. II.14 Ultrasound imaging. (a) Under the control of a computer. (b) Echoes arise when a pulse traveling along a spring is partly reflected at a juncture with a different type of spring. [17]

There are a wide range of applications of ultrasound imaging as a result of its non-invasive, non-ionizing nature, and its ability to form real-time axial and three-dimensional images. The tissues of interest need to reflect sufficient ultrasound energy; this limits the method to soft tissues, fluids and small calcifications preferably close to the surface of the body and unobstructed by bony structures. [20]

➤ Images from ultrasonography:

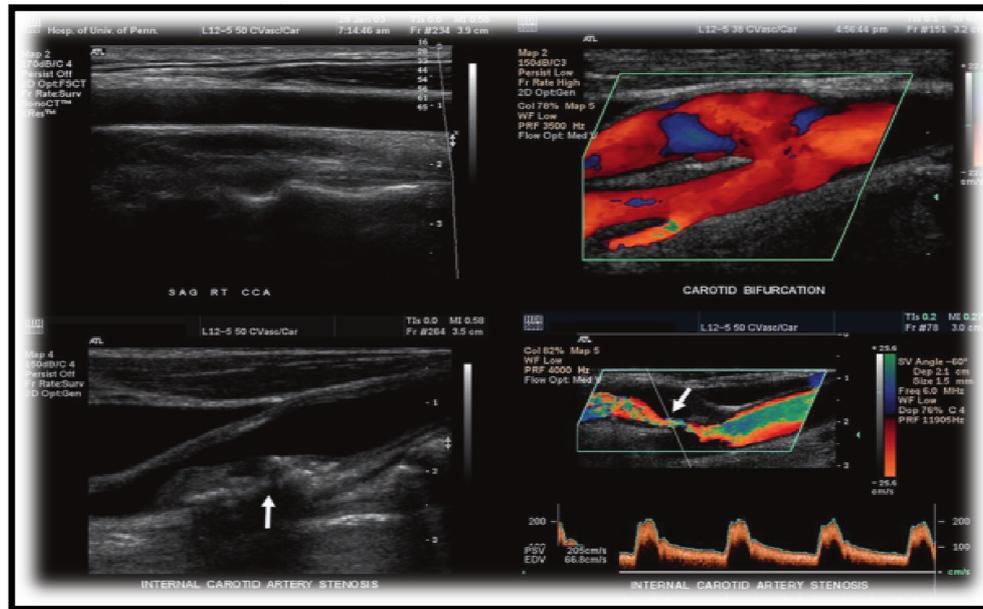


Fig. II.15 Ultrasound images of carotid artery. The two top figures show a normal gray-scale on the left and a normal color Doppler of the carotid bifurcation. The lower left gray-scale image shows arteriosclerotic plaque and debris. The color Doppler on the right indicates the marked degree of stenosis (arrows). [15]

II.2.2.2 Magnetic resonance imaging (MRI):

Sixty years after the first demonstration of nuclear magnetic resonance in condensed phase, and over three decades after the first cross-sectional image was published, magnetic resonance imaging (MRI) has without doubt evolved into the richest and most versatile biomedical imaging technique today. [15]

MRI is a wholly tomographic technique, just like X-ray CT, but it has no associated ionising radiation hazard. It provides a wider range of contrast mechanisms than X-rays and very much better spatial resolution in many applications. The extremely rapid development of MRI has been possible because it uses many of the techniques of its parent, nuclear magnetic resonance (NMR). In fact, in its infancy, MRI was called Spatially Localised Nuclear Magnetic Resonance but this was changed to magnetic resonance imaging (MRI) or simply MR both to avoid the long-winded title and to remove any misplaced association with ionising radiation through the adjective nuclear, developed by physicists in the 1940s, was first utilized for imaging the human body in the late 1970s. [3]

MRI is surely the most celebrated of the newer imaging modalities, and it is one of the most sophisticated imaging techniques. It can display high-quality slice and 3D images of the anatomy and physiology of tissues, organs, and vessels with in-plane resolution of under 1 mm, and comparable plane thicknesses. It provides contrast among radiologically similar soft tissues that is positively brilliant (Figure II.16). And it does all of this with no exposure of patient or staff to ionizing radiation. [17]

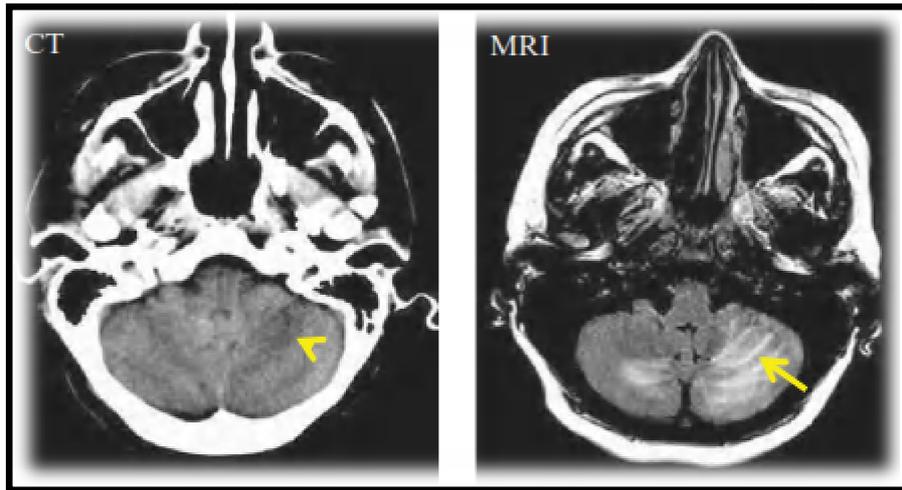


Fig. II.16 Two transverse slices of the same patient at the level of the posterior fossa, (a) Unenhanced CT axial reconstruction. (b) Unenhanced MRI FLAIR sequence axial reconstruction at the same level. [17]

➤ **The MRI system (hardware):**

A modern MRI system (Figure II.17) consists of three major pieces of highly specialized hardware, plus a computer: The patient is immersed in the very strong, constant, highly uniform *principal magnetic field*, in this case generated by a horizontally aligned superconducting magnet.

Three *gradient field* electromagnet coils are energized intermittently by the gradient drivers.

The radiofrequency (RF) electronics and coils generate and radiate brief pulses of electromagnetic energy, centered at or about the Larmor frequency, that penetrate into the patient. The same coils (or others that are placed directly against the patient's body for greater sensitivity) then sense the weak resonance echo signals produced immediately by the body.

The precise timing and shaping of the RF pulses and of the gradient fields are determined by the pulse programmer, which itself is under computer control. When not

running the procedures involved in generating and acquiring the raw MRI data, the computer performs the separate tasks of analyzing the data and reconstructing and processing images for display. It normally prepares images in the DICOM format for entry into a PACS. [17]

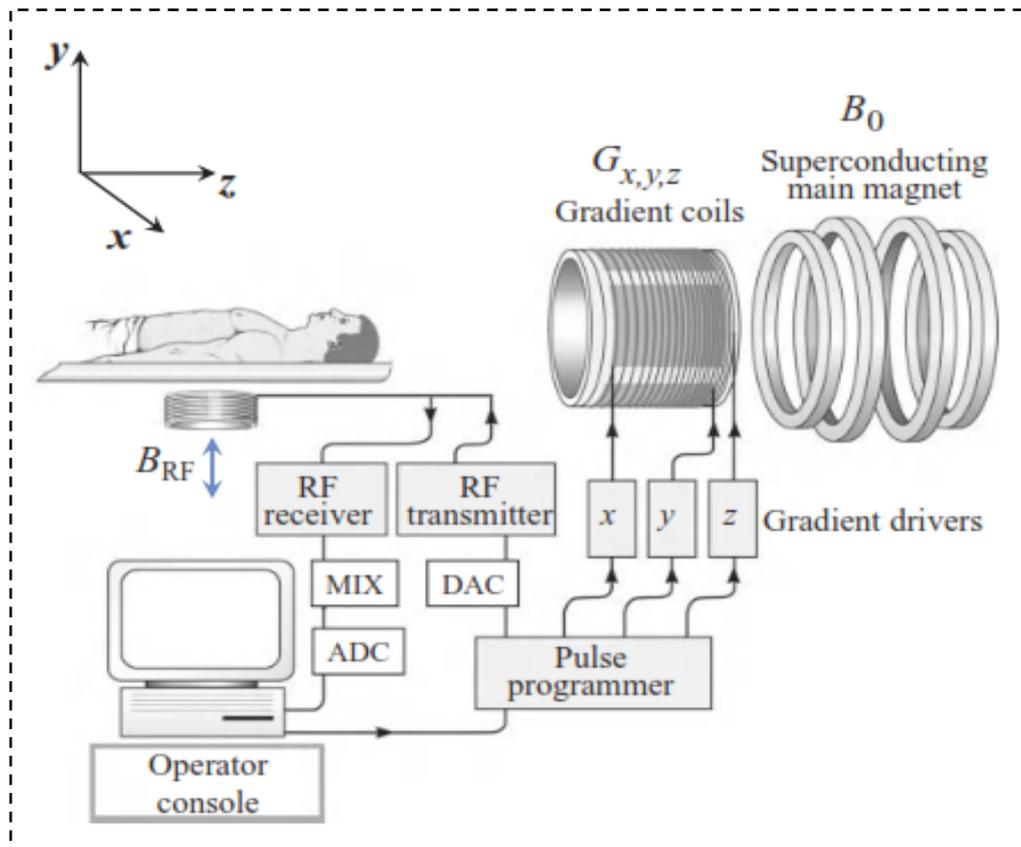


Fig. II.17 In a superconducting MRI device [7][17][21]

➤ Contrast in MRI:

Image contrast may be weighted to demonstrate different anatomical structures or pathologies. Each tissue returns to its equilibrium state after excitation by the independent processes of T1 (spin-lattice) and T2 (spin-spin) relaxation. [22]

✓ Spin Relaxation, T1 and T2 :

Now we must include the frictional forces that damp the motion of M after the tipping pulse. Friction, in this classical model, is caused by the interaction with the molecular fields characterized by T1, T2. The T1 process can be thought of as forcing M back into the Z direction, the T2 process effectively breaks M into its constituent parts. Both cause the oscillating signal to decay with time, see Figure II.18. [15]

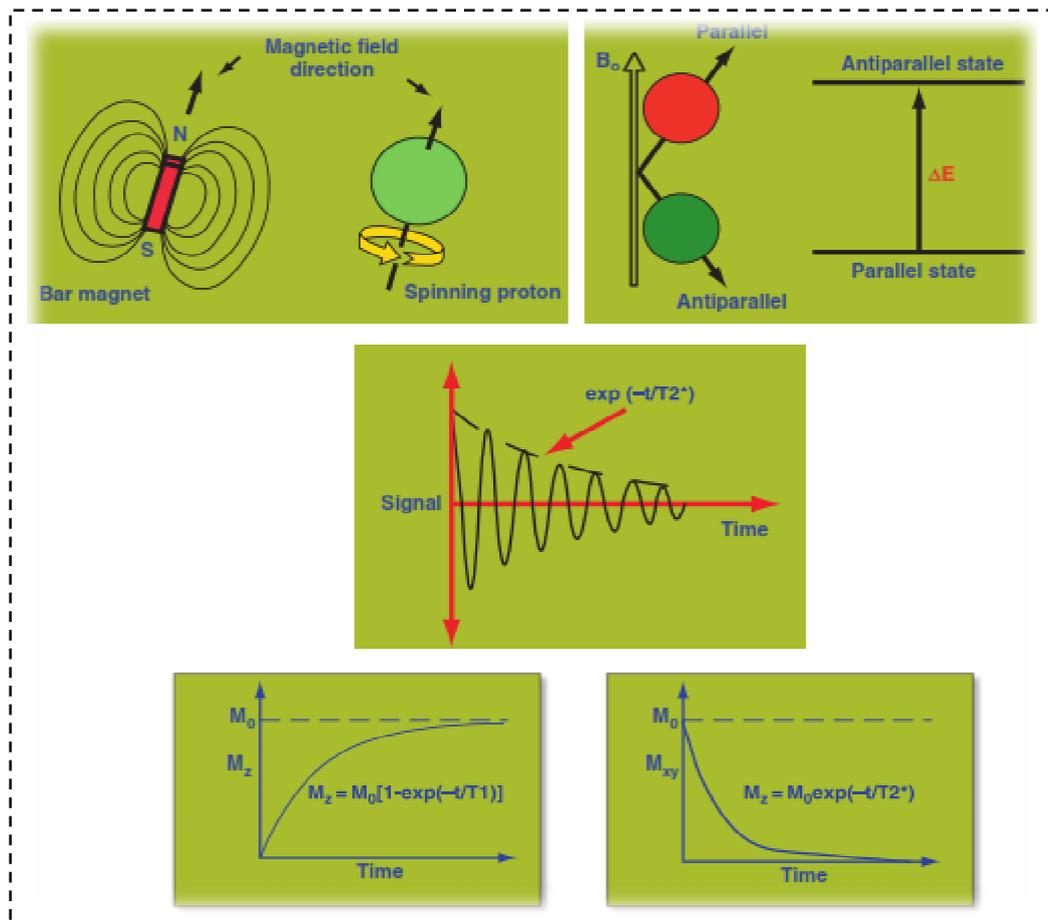


Fig. II.18. Nuclear magnetic resonance: *nuclear spins*, *RF* excite/detect signal, *T1* and *T2* exponential decay. [15]

➤ **Functional MRI (fMRI):**

Functional magnetic resonance imaging, or fMRI, is a technique for measuring brain activity. It works by detecting the changes in blood oxygenation and flow that occur in response to neural activity – when a brain area is more active it consumes more oxygen and to meet this increased demand blood flow increases to the active area. fMRI can be used to produce activation maps showing which parts of the brain are involved in a particular mental process, like is shown in;

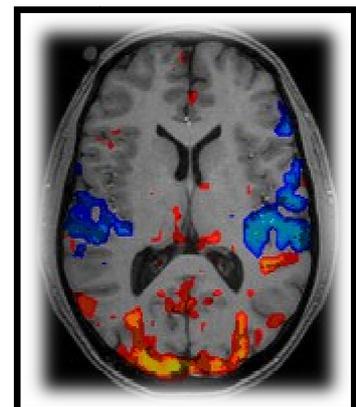


Fig. II.19 simplest kind of fMRI experiment [23]

As a brain imaging technique fMRI has several significant advantages:

1. It is non-invasive and doesn't involve radiation, making it safe for the subject.
2. It has excellent spatial and good temporal resolution.
3. It is easy for the experimenter to use.

The attractions of *fMRI* have made it a popular tool for imaging normal brain function – especially for psychologists. Over the last decade it has provided new insight to the investigation of how memories are formed, language, pain, learning and emotion to name but a few areas of research. *fMRI* is also being applied in clinical and commercial settings. [23]

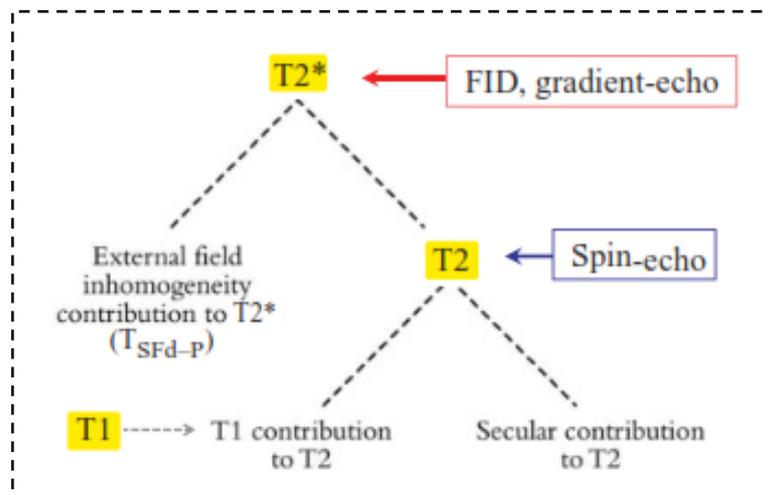


Fig. II.20 The complete spin-relaxation family tree. [17]

➤ **Images from MRI:**

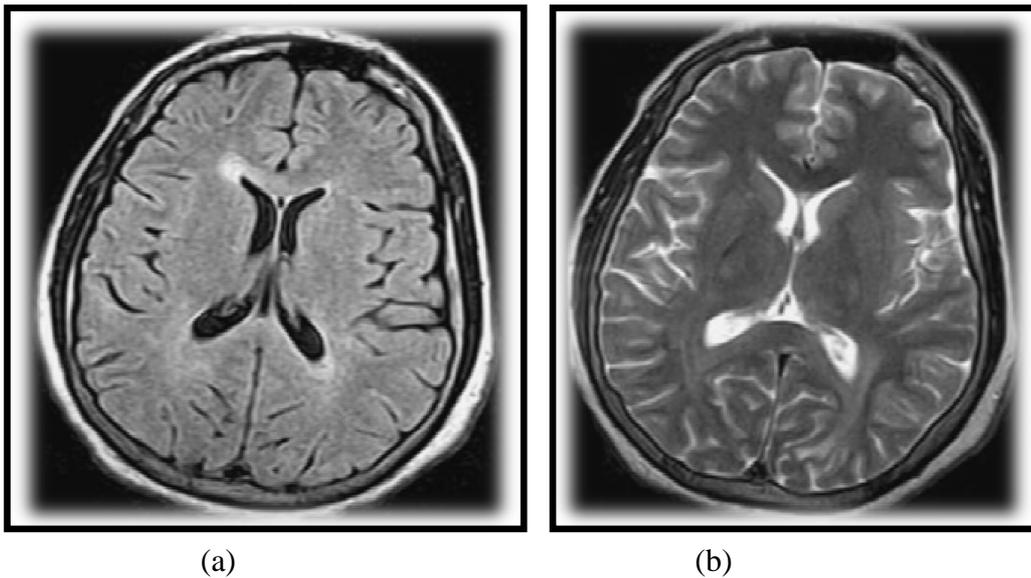


Fig. II.21 (a) T1-weighted spin echo image of the head. (b) T2-weighted spin echo image of the head. [7]

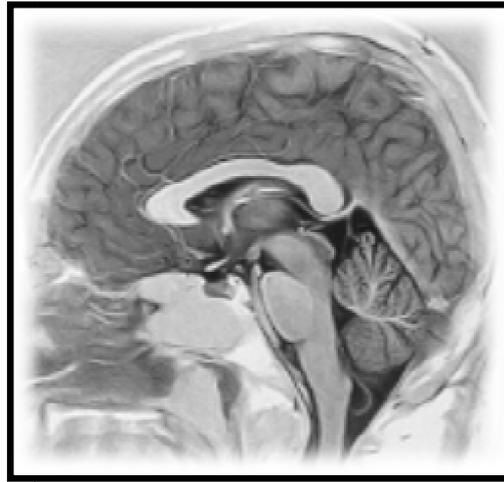


Fig. II.22. High resolution sagittal MRI brain image (Philips). [15]

II.3 Our exposure to ionizing Radiation:

In the earliest days, those who experimented with X-rays and radium were largely unaware of the harm that ionizing radiation can cause. The radiation induced effect observed most commonly among those pioneers was a reddening of skin; some even used this *erythema* to gauge X-ray exposure. But many cases of severe and irreversible radiogenic burns and carcinomas of the dermis were soon reported. And over the years, physicians and others have provided extensive and tragic evidence of the dangers of excessive irradiation.

Until recently, most of the ionizing radiation to which we are all exposed was naturally occurring. [17]

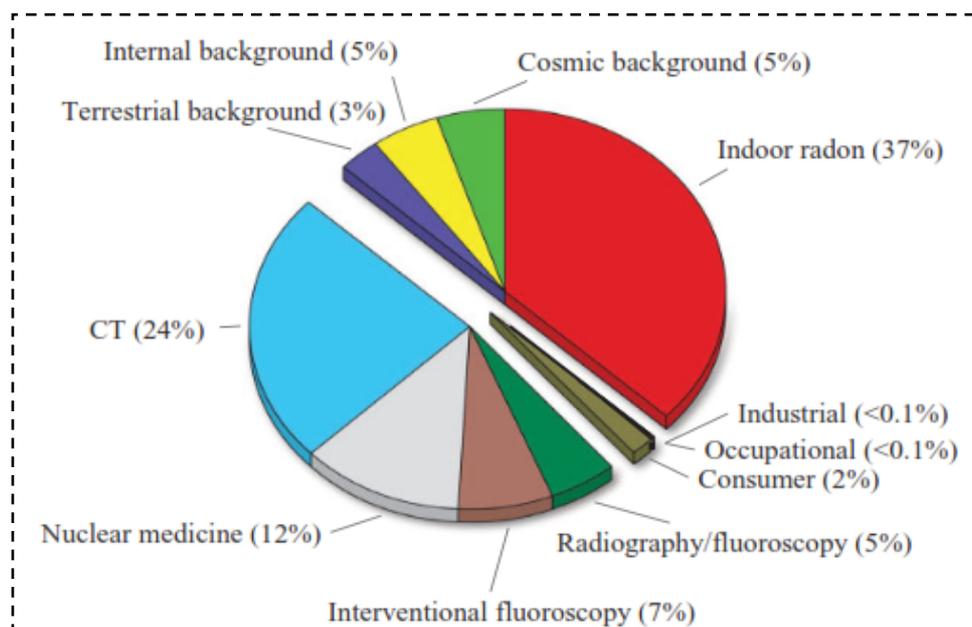


Fig. II.23 Relative contributions from natural background, medical, and other sources [17]

✚ Biologic Effects of X-Rays:

The biologic effects of x-irradiation are due to the recoiling electrons produced by the absorption or scattering of the incident x-rays, these electrons having enough kinetic energy to ionize hundreds of atoms along their trajectory. These electrons may damage DNA molecules directly or produce free radicals that can chemically damage genetic material; either effect may result in cell death or mutation. Magnetic resonance imaging and ultrasonic imaging do not utilize ionizing radiation, and there is no significant evidence that any biologic damage results from these imaging modalities. [17]

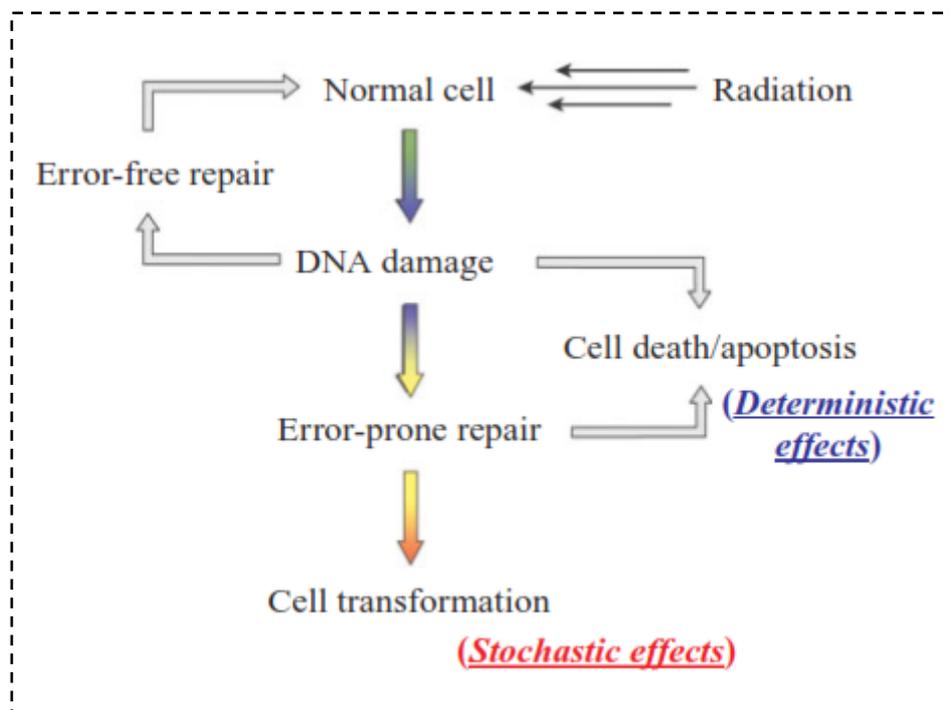


Fig. II.24 Sequence of events in the radiation damage in cells. [17]

✚ Effect on the Patient:

The primary risk to patients undergoing medical x-ray examinations is radiation induced cancer, primarily leukemia, thyroid, breast, lung, and gastrointestinal cancer. These relative risks are considered to be related to radiation dose and effective dose, which is essentially the exposure to various critical organs multiplied by an organ weighing factor. (The units of radiation dose or exposure a rem, a rad, and a roentgen are essentially equivalent for x- and gamma-ray irradiation.)

The Pregnant Patient:

The fetus consists of rapidly dividing cells and hence is more sensitive to radiation, particularly in the first trimester. The principal risks to the fetus from *in utero* irradiation are cancer induction, malformation (e.g., small head size), or mental retardation.

Every fertile female patient should be asked if she might be pregnant; if so, the relative risks of the diagnostic x-ray procedure versus the expected benefit should be weighed before the procedure is performed, or alternate imaging procedures such as MR imaging or ultrasound should be considered. Note, however, that the added risk from diagnostic xray procedures is generally negligible compared to the normal risks of pregnancy, because fetal doses are typically below 5 rad in these procedures. [16]

II.4 Conclusion:

In conclusion, through our work in this chapter, it is now extremely clear to us that the creation and evolution of Medical Imaging has been critical to modern medicine and medical research. Without medical imaging, nothing would be known about the human body or issues surrounding it without evasive surgery. It is the basis of modern medicine, diagnosis of certain things would be near impossible without Medical Imaging technologies like X-Ray, Computer Tomography and MRI scans, unless dangerous surgery would be conducted. Medical and scientific research would be extremely limited without being able to see the incredibly small 'building blocks' that make up everything. Machines like the Synchrotron allow this to happen and gained humans knowledge that is priceless. With Medical Imaging, diseases can be easier to cure than ever before. The development of Medical Imaging looks like it can only improve in the future. With so advanced technology like Free-electron Lasers and the synchrotron, you could not say that there is no chance any disease cannot be cured. Medical Imaging has and will save millions of lives, possibly billions.

We will study in the third chapter numerical analysis, linear regression and statistical study using the analysis of variance, or more briefly ANOVA.

CHAPTER III

Theoric of Numerical

&

Statistical methods

III.1 Introduction:

In numerical analysis, the Runge–Kutta (RK) methods (German pronunciation: [ˌʁʊŋəˈkʊtʌ]) are an important family of implicit and explicit iterative methods for the approximation of solutions of ordinary differential equations. These techniques were developed around 1900 by the German mathematicians C. Runge and M. W. Kutta. [24]

Regression and analysis of variance are probably the most frequently applied of all statistical analyses. Regression and analysis of variance are used extensively in many areas of research, such as psychology, biology, medicine, education, sociology, anthropology, economics, political science, as well as in industry and commerce.

Regression emerged in biology and psychology towards the end of the 19th century, as scientists studied the correlation between people's attributes and characteristics. It allows examination of the relationships between an unlimited number of predictor variables and a response or dependent variable, and enables values on one variable to be predicted from the values recorded on one or more other variables. [25]

Analysis of variance became widely known after being included in Fisher's 1925 book. *Statistical methods for research workers*. In statistics, analysis of variance (ANOVA) is a collection of statistical models, and their associated procedures, in which the observed variance in a particular variable is partitioned into components attributable to different sources of variation. In its simplest form, ANOVA provides a statistical test of whether or not the means of several groups are all equal, and therefore generalizes t-test to more than two groups. Doing multiple two-sample t-tests would result in an increased chance of committing an error. For this reason, ANOVAs are useful in comparing two, three, or more means. [26]

In this chapter, we translate non linear model to linear one by using numerical analysis: “Runge-Kutta 4 (RK4)” before pass to the statistical study where we used the Regression then Anova technique to extract the place of the lesion on MRI image.

As problematic what's the meaning of Runge kutta? What it the result of it? What's the main of the regression and how do we pass to Anova technique? All these questions will be more explain in the following titles. But we can't pass to Runge-Kutta and all of that, before we talk about the ordinary differential equations, at least a small background of it, because the Runge-Kutta method is the most basic explicit method for numerical integration of ordinary differential equations (ODEs).

III.2 Background of ordinary differential equations:

Differential equations are one of the most important mathematical tools used in modeling problems in physical sciences. Historically, differential equations (DE) have originated in chemistry, physics and engineering. More recently, they have also arisen in medicine, biology, anthropology, and the like. Ordinary differential equations arise frequently in the study of physical systems. Unfortunately, many cannot be solved exactly. This is why the ability to numerically approximate these methods is so important [27].

In mathematics, an **ordinary differential equation** or **ODE** is an equation containing a function of one independent variable and its derivatives. The term "*ordinary*" is used in contrast with the term partial differential equation which may be with respect to more than one independent variable.

Ordinary differential equations (ODEs) arise in many different contexts throughout mathematics and science (social and natural) one way or another, because when describing changes mathematically, the most accurate way uses differentials and derivatives (related, though not quite the same). Since various differentials, derivatives, and functions become inevitably related to each other via equations, a differential equation is the result, describing dynamical phenomena, evolution, and variation. Often, quantities are defined as the rate of change of other quantities (time derivatives), or gradients of quantities, which is how they enter differential equations. [28]

In general, it will not be possible to find exact, analytic solutions to the ODE. However, it is possible to find an approximate solution with a finite difference scheme such as Euler and Runge-Kutta methods. [29]

The first method we shall study for solving differential equations is called ***Euler's method***, it serves to illustrate the concepts involved in the advanced methods. It has limited use because of the larger error that is accumulated with each successive step. However, it is important to study Euler's method because the remainder term and error analysis is easier to understand. [30]

An Historical Perspective

When ***Euler*** [31] proposed his method,

$$y_{n+1} = y_n + hk_1 \quad (\text{Equ.III.1})$$

where $k_1 = f(x_n, y_n)$

It represented the simplest method available to numerically approximate the solution of an ordinary differential equation.

In the formulation of equation (III.1) we note that:

- y_{n+1} depends explicitly on y_n but on no earlier of y_n, y_{n-1}, \dots
- the function f is evaluated only once in the step from the computation of y_n to the computation of y_{n+1} ;
- only the function f itself is used rather than f_2, f_3, \dots say which yield values of $y''(x)$, $y'''(x)$, in terms of $y(x)$ or of f' (the Jacobian of f), f'' , ...

Euler method is both one-step and multi-step, and this fact together with the stability requirements, can mean that h has to be chosen to be very small and as noted in, “the method of Euler is ideal as an object of theoretical study but unsatisfactory as a means of obtaining accurate results”. Due to the low accuracy and poor stability behavior, generalizations have been made to the method of Euler. [31]

Euler’s method give rise to a rather inefficient approximation of the integral by the area of a rectangle of height $f(x_0)$; (see Fig. III.1)

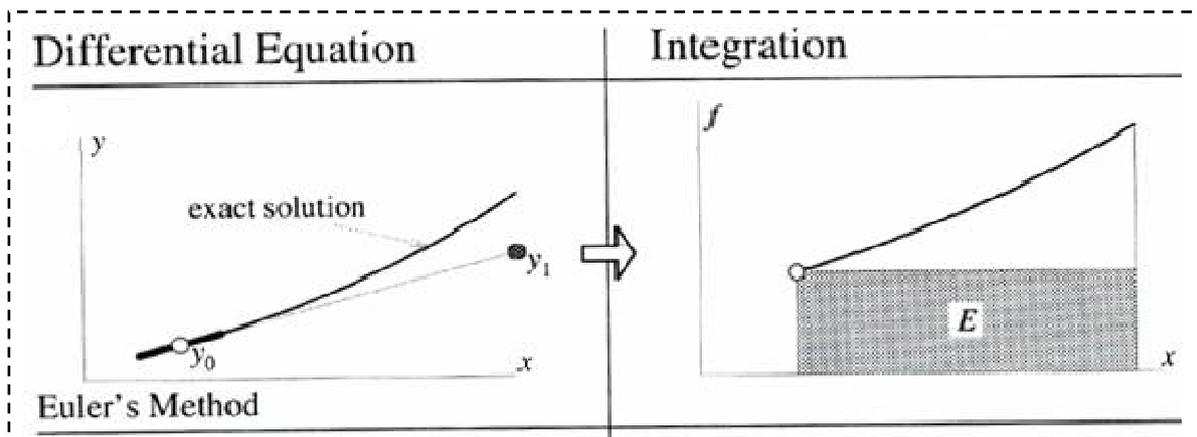


Fig. III.1 Runge’s motivation culled from [32]

III.3 The Runge-Kutta methods:

III.3.1 Basic Runge-Kutta methods:

Runge-Kutta methods have the advantage of being one-step methods, possibly having high order and good stability properties, and therefore they (and related methods) are quite popular.

To settle notation we recapitulate the form of the Runge-Kutta method. For the autonomous explicit ODE system

$$\mathbf{y}' = \mathbf{f}(\mathbf{y}) \quad (\text{Equ. III.2})$$

The method, for advancing the solution from a point \mathbf{y}_n to the next, would look like this:

$$\mathbf{Y}_{n,j} = \mathbf{y}_n + h \sum_{i=1}^s a_{ij} \mathbf{f}(\mathbf{Y}_{n,i}), i = 1, 2, \dots, s \quad (\text{Equ. III.3a})$$

$$\mathbf{y}_{n+1} = \mathbf{y}_n + h \sum_{i=1}^s b_i \mathbf{f}(\mathbf{Y}_{n,i}) \quad (\text{Equ. III.3b})$$

The method is a one-step method (i.e. it does not utilize information from previous steps) and it is specified by the matrix \mathbf{A} with the elements a_{ij} , and the vector \mathbf{b} having the elements b_i . We call the $\mathbf{Y}_{n,i}$'s the internal stages of the step. In general these equations represent a non-linear system of equations.

The classical theory for determining the order of the local and global error is found in a number of books on ODEs. Both the J. C. Butcher and P. Albrecht approach are shortly described in [Lam91]. [33]

III.3.2 Fourth-order Runge-Kutta method:

Explicit Runge-Kutta methods are popular as each stage can be calculated with one function evaluation. In contrast, implicit *Runge-Kutta methods* usually involve *solving a non-linear system of equations* in order to evaluate the stages. As a result, explicit schemes are much less expensive to implement than implicit schemes.

However, there are cases in which implicit schemes are necessary and that is in the case of stiff sets of equations.

The higher-order Runge-Kutta methods can be derived in manner similar to the midpoint formula. An s-stage method is compared to a Taylor method and the terms are matched up to the desired order.

Methods of order $M > 4$ require $M + 1$ or $M + 2$ function evaluations or stages, in the case of explicit Runge-Kutta methods. As a result, fourth-order Runge-Kutta methods have achieved great popularity over the years as they require only four function evaluations per step. In particular, there is the classic fourth-order Runge-Kutta formula:

$$\left\{ \begin{array}{l} k_1 = hf(t_n, x_n) \\ k_2 = hf\left(t_n + \frac{h}{2}, x_n + \frac{k_1}{2}\right) \\ k_3 = hf\left(t_n + \frac{h}{2}, x_n + \frac{k_2}{2}\right) \\ k_4 = hf(t_n + h, x_n + k_3) \\ x_{n+1} = x_n + \frac{1}{6}(k_1 + 2k_2 + 2k_3 + k_4) \end{array} \right. \quad (\text{Equ. III.4})$$

So only first order ordinary differential equations can be solved by using the Runge-Kutta 4th order method. In other sections, *Euler and Runge-Kutta methods are used to solve higher order ordinary differential equations or coupled (simultaneous) differential equations.* [25]

III.3.3 Runge-Kutta for coupled systems (two-variables):

The Runge-Kutta algorithm can be easily extended to a set of first order differential equations. You wind up with essentially the same formulas shown above, but all the variables (except for time) are vectors.

To give an idea of how it works, here is an example where we expand the vector notation. That is, instead of using the highly compact vector notation, we write out all the components of the vector.

Suppose there are only two variables, x , y and two differential equations. For our (general) problem from class

$$\frac{dx}{dt} = f(t, x, y), \quad x(t_0) = x_0$$

$$\frac{dy}{dt} = g(t, x, y), \quad y(t_0) = y_0$$

we get our approximate solution (x_n, y_n) at time $t_n = 1, 2, \dots$ via the iteration of

$$\left\{ \begin{array}{l} x_{n+1} = x_n + \frac{h}{6}(k_{n1} + 2k_{n2} + 2k_{n3} + k_{n4}) \\ y_{n+1} = y_n + \frac{h}{6}(l_{n1} + 2l_{n2} + 2l_{n3} + l_{n4}) \end{array} \right. \quad (\text{Equ. III.5})$$

where the formulas for each of the k 's and l 's are

$$\left\{ \begin{array}{l} k_{n1} = f(t_n, x_n, y_n) \\ l_{n1} = g(t_n, x_n, y_n) \\ k_{n2} = f\left(t_n + \frac{h}{2}, x_n + \frac{h}{2}k_{n1} + y_n + \frac{h}{2}l_{n1}\right) \\ l_{n2} = g\left(t_n + \frac{h}{2}, x_n + \frac{h}{2}k_{n1} + y_n + \frac{h}{2}l_{n1}\right) \\ k_{n3} = f\left(t_n + \frac{h}{2}, x_n + \frac{h}{2}k_{n2} + y_n + \frac{h}{2}l_{n2}\right) \\ l_{n3} = g\left(t_n + \frac{h}{2}, x_n + \frac{h}{2}k_{n2} + y_n + \frac{h}{2}l_{n2}\right) \\ k_{n4} = f(t_n + h, x_n + hk_{n3} + y_n + hl_{n3}) \\ l_{n4} = g(t_n + h, x_n + hk_{n3} + y_n + hl_{n3}) \end{array} \right. \quad (\text{Equ. III.6})$$

Given starting values x_0, y_0 we can plug them into the formula to find x_1, y_1 . Then we can plug in x_1, y_1 to find x_2, y_2 and so on. [34] [35] [36]

III.3.4 Examples:

Runge-Kutta 4th order method is a numerical technique used to solve ordinary differential equation of the form:

$$\frac{\partial y}{\partial t} = f(x, y), y(0) = y_0$$

- **Example 1:**

Rewrite

$$\frac{dy}{dx} + 2y = 1.3e^{-x}, y(0) = 5$$

In

$$\frac{dy}{dx} = f(x, y), y(0) = y_0$$

- **Solution:**

$$\frac{dy}{dx} + 2y = 1.3e^{-x}, y(0) = 5$$

$$\frac{dy}{dx} = 1.3e^{-x} - 2y, y(0) = 5$$

In this case

$$f(x, y) = 1.3e^{-x} - 2y$$

- **Example 2:**

A ball at 1200 K is allowed to cool down in air at an ambient temperature of 300 K. Assuming heat is lost only due to radiation, the differential equation for the temperature of the ball is given by

$$\frac{d\theta}{dt} = -2.2067 \times 10^{-12}(\theta^4 - 81 \times 10^8) \quad , \theta(0) = 1200 \text{ K}$$

Where θ is in K and t in seconds. Find the temperature at $t = 480$ seconds using Runge-Kutta 4th order method. Assume a step size of $h=240$ seconds.

- **Solution:**

$$\frac{d\theta}{dt} = -2.2067 \times 10^{-12}(\theta^4 - 81 \times 10^8)$$

$$f(t, \theta) = -2.2067 \times 10^{-12}(\theta^4 - 81 \times 10^8)$$

$$\theta_{i+1} = \theta_i + \frac{1}{6}(k_1 + 2k_2 + 2k_3 + k_4)h$$

For $i = 0$, $t_0 = 0$, $\theta_0 = 1200 \text{ K}$

$$\begin{aligned} k_1 &= f(t_0, \theta_0) \\ &= f(0, 1200) \\ &= -2.2067 \times 10^{-12}(1200^4 - 81 \times 10^8) \\ &= -4.5579 \end{aligned}$$

$$\begin{aligned} k_2 &= f\left(t_0 + \frac{1}{2}h, \theta_0 + \frac{1}{2}k_1h\right) \\ &= f\left(0 + \frac{1}{2}(240), 1200 + \frac{1}{2}(-4.5579) \times 240\right) \\ &= f(120, 653.05) \\ &= -2.2067 \times 10^{-12}(653.05^4 - 81 \times 10^8) \\ &= -0.38347 \end{aligned}$$

$$\begin{aligned} k_3 &= f\left(t_0 + \frac{1}{2}h, \theta_0 + \frac{1}{2}k_2h\right) \\ &= f\left(0 + \frac{1}{2}(240), 1200 + \frac{1}{2}(-0.38347) \times 240\right) \\ &= f(120, 1154) \\ &= -2.2067 \times 10^{-12}(1154^4 - 81 \times 10^8) \end{aligned}$$

$$= -3.8954$$

$$k_4 = f(t_0 + h, \theta_0 + k_3 h)$$

$$= f(0 + 240, 1200 + (-3.894) \times 240)$$

$$= f(240, 265.10)$$

$$= -2.2067 \times 10^{-12} ((265.10)^4 - 81 \times 10^8)$$

$$= 0.0069750$$

$$\theta_1 = \theta_0 + \frac{1}{6}(k_1 + 2k_2 + 2k_3 + k_4)h$$

$$= 1200 + \frac{1}{6}(-4.5579 + 2(-0.38347) + 2(-3.8954) + (0.0069750)) \times 240$$

$$= 1200 + (-2.1848) \times 240$$

$$= 675.65 \text{ K}$$

θ_1 is the approximate temperature at

$$t = t_1$$

$$= t_0 + h$$

$$= 0 + 240$$

$$= 240$$

$$\theta_1 = \theta(240)$$

$$\approx 675.65 \text{ K}$$

For $i = 1$, $t_1 = 240$, $\theta_1 = 675.65 \text{ K}$

$$k_1 = f(t_1, \theta_1)$$

$$= f(240, 675.65)$$

$$= -2.2067 \times 10^{-12} ((675.65)^4 - 81 \times 10^8)$$

$$= -0.44199$$

$$k_2 = f\left(t_1 + \frac{1}{2}h, \theta_1 + \frac{1}{2}k_1 h\right)$$

$$= f\left(240 + \frac{1}{2}(240), 675.65 + \frac{1}{2}(-0.44199) \times 240\right)$$

$$= f(360, 622.61)$$

$$= -2.2067 \times 10^{-12} ((622.61)^4 - 81 \times 10^8)$$

$$= -0.31372$$

$$k_3 = f\left(t_1 + \frac{1}{2}h, \theta_1 + \frac{1}{2}k_2 h\right)$$

$$= f\left(240 + \frac{1}{2}(240), 675.65 + \frac{1}{2}(-0.31372) \times 240\right)$$

$$= f(360, 638)$$

$$= -2.2067 \times 10^{-12} (638^4 - 81 \times 10^8)$$

$$= -0.34775$$

$$k_4 = f(t_1 + h, \theta_1 + k_3 h)$$

$$= f(240 + 240, 675.65 + (-0.34775) \times 240)$$

$$= f(480, 592.19)$$

$$= -2.2067 \times 10^{-12} ((592.19)^4 - 81 \times 10^8)$$

$$= -0.25351$$

$$\theta_2 = \theta_1 + \frac{1}{6}(k_1 + 2k_2 + 2k_3 + k_4)h$$

$$= 675.65 + \frac{1}{6}(-0.44199 + 2(-0.31372) + 2(-0.34775) + (0.25351)) \times 240$$

$$= 675.65 + \frac{1}{6}(-2.0184) \times 240$$

$$= 594.91 \text{ K}$$

θ_2 is the approximate temperature at

$$t = t_2$$

$$= t_1 + h$$

$$= 240 + 240$$

$$= 480$$

$$\theta_2 = \theta(480)$$

$$\approx 594.91 \text{ K}$$

In Figure III.2 we are comparing the exact results with Euler's method (Runge-Kutta 1st order method), Heun's method (Runge-Kutta 2nd order method), and Runge-Kutta 4th order method.

The formula described in this chapter was developed by Runge. This formula is same as Simpson's 1/3 rule, if $f(x, y)$ were only a function of x . There are other versions of the 4th order method just like there are several versions of the second order methods. The formula developed by Kutta is

$$y_{i+1} = y_i + \frac{1}{6}(k_1 + 3k_2 + 3k_3 + k_4)h \quad (\text{Equ. III.7})$$

Where

$$k_1 = f(x_i, y_i) \quad (\text{Equ. III.8a})$$

$$k_2 = f\left(x_i + \frac{1}{3}h, y_i + \frac{1}{3}k_1 h\right) \quad (\text{Equ. III.8b})$$

$$k_3 = f\left(x_i + \frac{2}{3}h, y_i - \frac{1}{3}k_1 h + h k_2\right) \quad (\text{Equ. III.8c})$$

$$k_4 = f(x_i + h, y_i + k_1h - k_2h + k_3h) \quad (\text{Equ. III.8d})$$

This formula is the same as the Simpson's 3/8 rule, if $f(x, y)$ is only a function of x . [37]

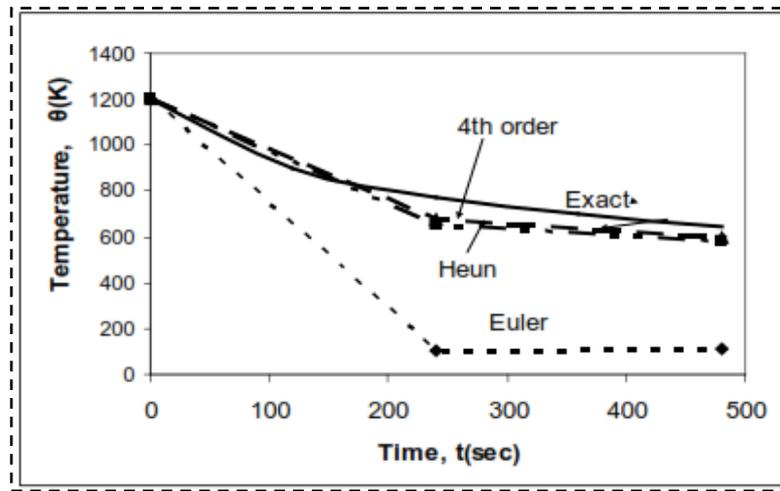


Fig. III.2 Comparison of Runge-Kutta methods of 1st (Euler), 2nd, and 4th order. [37]

After we translate the non linear model to linear one (solving a non-linear system of equations), then we study the linear regression and the fitted regression line for calculate at last Anova test as the following titles.

III.4 Regression analysis:

Regression analysis attempts to explain data (the dependent variable scores) in terms of a set of independent variables or predictors (the model) and a residual component (error). Typically, a researcher who applies regression is interested in predicting a quantitative dependent variable from one or more quantitative independent variables, and in determining the relative contribution of each independent variable to the prediction: there is interest in what proportion of the variation in the dependent variable can be attributed to variation in the independent variable(s). Regression also may employ categorical (also known as nominal or qualitative) predictors: the use of independent variables such as sex, marital status and type of teaching method is common. [25][38]

III.4.1 The two-variable linear model:

The two-variable linear model, or *simple regression analysis*, is used for testing hypotheses about the relationship between a dependent variable Y and an independent or explanatory variable X and for prediction. *Simple linear regression analysis* usually begins

by plotting the set of XY values on a scatter diagram and determining by inspection if there exists an approximate linear relationship:

$$Y_i = b_0 + b_1 X_i \quad (\text{Equ. III.9})$$

Since the points are unlikely to fall precisely on the line, the exact linear relationship in Eq. (III.4) must be modified to include a random disturbance, error, or stochastic term, u_i :

$$Y_i = b_0 + b_1 X_i + u_i \quad (\text{Equ. III.10})$$

The error term is assumed to be (1) normally distributed, with (2) zero expected value or mean, and (3) constant variance, and it is further assumed (4) that the error terms are uncorrelated or unrelated to each other, and (5) that the explanatory variable assumes fixed values in repeated sampling (so that X_i and u_i are also uncorrelated). Figure III.3 gives an illustration of data resulting from the simple linear regression model. [39]

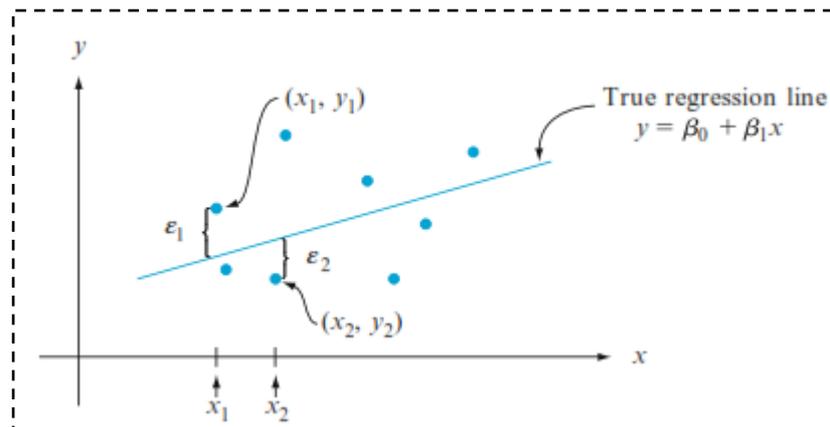


Fig. III.3 Points corresponding to observations from the simple linear regression model [39]

To check if there is a relationship between x and y , and if it does exist, can we describe it and use it to predict y from x ? The answer is yes, by applying the relation of covariance and using regression then fitting line using the least square solution, but before that we should first pass to the least square method.

III.4.2 The ordinary least-squares method:

The ordinary least-squares method (OLS) is a technique for fitting the “best” straight line to the sample of XY observations. It involves minimizing the sum of the squared (vertical) deviations of points from the line:

$$\text{Min } \sum (Y_i - \hat{Y}_i)^2 \quad (\text{Equ. III.11})$$

Where Y_i refers to the actual observations, and \hat{Y}_i refers to the corresponding fitted values, so that $Y_i - \hat{Y}_i = e_i$, the residual. This gives the following two normal equations:

$$\sum Y_i = nb_0 + \hat{b}_1 \sum X_i \quad (\text{Equ. III.12})$$

$$\sum X_i Y_i = \hat{b}_0 \sum X_i + \hat{b}_1 \sum X_i^2 \quad (\text{Equ. III.13})$$

where n is the number of observations and \hat{b}_0 and \hat{b}_1 are estimators of the true parameters b_0 and b_1 . Solving simultaneously Eqs. (III.8) and (III.9), we get:

$$\hat{b}_1 = \frac{n \sum X_i Y_i - \sum X_i \sum Y_i}{n \sum X_i^2 - (\sum X_i)^2} \quad (\text{Equ. III.14})$$

The value of \hat{b}_0 is then given by

$$\hat{b}_0 = \bar{Y} - \hat{b}_1 \bar{X} \quad (\text{Equ. III.15})$$

It is often useful to use an equivalent formula for estimating \hat{b}_1 :

$$\hat{b}_1 = \frac{\sum x_i y_i}{\sum x_i^2} = \frac{\text{cov}(X, Y)}{\sigma_X^2} \quad (\text{Equ. III.16})$$

where $x_i = X_i - \bar{X}$, and $y_i = Y_i - \bar{Y}$. The estimated least-squares regression (OLS) equation is then:

$$\hat{Y}_i = \hat{b}_0 + \hat{b}_1 X_i \quad (\text{Equ. III.17})$$

III.4.3 Test of goodness of fit and correlation:

In many situations the objective in studying the joint behavior of two variables is to see whether they are related, rather than to use one to predict the value of the other. [39]

We can achieve that by the following relationship: “*The relation of covariance*”

$$\text{cov}(x, y) = \frac{\sum_{i=1}^n (x_i - \bar{x})(y_i - \bar{y})}{n - 1} \quad (\text{Equ. III. 18})$$

What is the strength of this relationship? Pearson’s role said: [40]

Covariance does not really tell us anything but we can measure the standardises the covariance value, and Divides the covariance by the multiplied standard deviations of X and Y : (3.19)

The closer observations fall to the regression line (i.e., the smaller the residuals), the greater is the variation in Y “explained” by the estimated regression equation. The total variation in Y is equal to the explained plus the residual variation:

$$\sum (Y_i - \bar{Y})^2 = \sum (\hat{Y}_i - \bar{Y})^2 + \sum (Y_i - \hat{Y}_i)^2$$

Total variation *Explained variation* *Residual variation*
in Y [or total sum *in Y [or regression* *in Y [or error sum*
of squares *sum of squares* *of squares*
(TSS)] *(RSS)]* *(ESS)]*

(Equ.III.19)

Dividing both sides by TSS gives

$$1 = \frac{RSS}{TSS} + \frac{ESS}{TSS}$$

The coefficient of determination, or R^2 , is then defined as the proportion of the total variation in Y “explained” by the regression of Y on X :

$$R^2 = \frac{RSS}{TSS} = 1 - \frac{ESS}{TSS}$$

(Equ. III.20)

R^2 can be calculated by

$$R^2 = \frac{\sum \hat{y}_i^2}{\sum y_i^2} = 1 - \frac{\sum e_i^2}{\sum y_i^2}$$

(Equ. III.21)

where

$$\sum \hat{y}_i^2 = \sum (\hat{Y}_i - \bar{Y}_i)^2$$

(Equ. III.22)

R^2 ranges in value from 0 (when the estimated regression equation explains none of the variation in Y to 1 (when all points lie on the regression line).

The correlation coefficient r is given by:

$$r = \sqrt{R^2} = \frac{cov(X,Y)}{\sigma_X \sigma_Y} = \sqrt{\hat{b}_1 \frac{\sum x_i y_i}{\sum y_i^2}}$$

(Equ. III.23)

r ranges in value from -1 (for perfect negative linear correlation) to $+1$ (for perfect positive linear correlation) and does not imply causality or dependence. With qualitative data, the *rank* or (*the Spearman*) *correlation coefficient* r' can be used. [41]

And last but not least, we pass to the ANOVA, and all of the things they related to it. Such as the F test for testing the null hypothesis that the population means are identical, and...etc

III.5 Review of the R. A. Fisher's Statistical Methods for Research Workers:

R. A. Fisher's *Statistical Methods for Research Workers* (1925) [42] was probably the most influential statistics book of the 20th century. It presented in book form for the first time Fisher's work on maximum likelihood, t -tests (including applications to regression), the z -transformation of the correlation coefficient, *the analysis of variance*, randomization and blocking in the design of experiments, etc. [42] [43]

III.6 Understanding the analysis of variance:

The analysis of variance, or more briefly ANOVA, refers broadly to a collection of statistical procedures for the analysis of quantitative responses. The simplest ANOVA problem is referred to variously as a single-factor, single-classification, or one-way ANOVA and involves the analysis of data sampled from two or more numerical populations (distributions). [41][43]

III.6.1 Basics of ANOVA:

Single-factor ANOVA focuses on a comparison of two or more populations. Let

I = the number of treatments being compared

μ_1 = the mean of population 1 (or the true average response when treatment 1 is applied)

⋮

μ_I = the mean of population I (or the true average response when treatment I is applied)

Then the hypotheses of interest are

$$H_0 = \mu_1 = \mu_2 = \dots = \mu_I$$

Versus

H_a : at least two of the μ_i 's different

If $I = 4$, H_0 is true only if all four μ_i 's are identical. H_a would be true, for example, if $\mu_1 = \mu_2 \neq \mu_3 = \mu_4$, if $\mu_1 = \mu_3 = \mu_4 \neq \mu_2$, or if all four μ_i 's differ from each other.

A test of these hypotheses requires that we have available a random sample from each population or treatment. [39]

III.6.2 The null hypothesis:

We will test the null hypothesis that there is no difference between the various groups (conditions). We can state that null hypothesis like this: [44]

$$H_0: \mu_1 = \mu_2 = \mu_3 = \mu_4 = \mu_5 = \mu \quad (\text{Equ. III.24})$$

In other words, the null hypothesis is that all means are equal to each other and to the grand mean (μ), and that all treatment (group) effects are zero.

III.6.3 The assumptions of ANOVA:

The I population or treatment distributions are all normal with the same variance σ^2 . That is, each X_{ij} is normally distributed with; [39]

$$E(X_{ij}) = \mu_i \quad ; \quad V(X_{ij}) = \sigma^2 \quad (\text{Equ. III.25})$$

III.6.4 Calculating SS_{total} , $SS_{treatments}$ and SS_{error} :

First, we calculate SS_{total} ('total sum of squares') — the sum of squares of all the observations (the *summed squared deviations of each observation from the overall mean*), regardless of which treatment group the observations came from. [44]

$$SS_{total} = \sum(x - \bar{x})^2 \quad \left(= \sum x^2 - \frac{(\sum x)^2}{N} \right) \quad (\text{Equ. III.26})$$

Now we calculate $SS_{treatment}$. This represents the *summed squared deviations of the treatment mean from the mean of all treatment means, summed over each data point*. (Or, in terms of totals, the summed squared deviations of each total $[T_j]$ from the mean of the treatment totals $[\bar{T}]$, all divided by the number of observations per total.)

$$SS_{treatment} = \sum n(\bar{x}_i - \bar{x})^2 \quad (\text{Equ.III.27})$$

$$\left(\begin{aligned} &= \sum n \left(\frac{T_i - \bar{T}}{n} \right)^2 = \sum \frac{n}{n^2} (T_i - \bar{T})^2 \\ &= \frac{\sum (T_i - \bar{T})^2}{n} \\ &= \frac{\sum T_i^2 - \frac{(\sum T_i)^2}{a}}{n} = \frac{\sum T_i^2}{n} - \frac{(\sum T_i)^2}{na} \\ &= \frac{\sum T_i^2}{n} - \frac{(\sum x)^2}{N} \end{aligned} \right)$$

Where a is the number of treatments, n is the number of observations per treatment, and N is the total number of observations ($= na$).

Now we can calculate SS_{error} . This represents the sum of the squared deviations of each point from its group mean. Since $SS_{total} = SS_{treatment} + SS_{error}$, the quick way to obtain SS_{error} is by subtraction:

$$SS_{error} = \sum (x - \bar{x}_i)^2 = SS_{total} - SS_{treatment} \quad (\text{Equ. III.28})$$

Alternatively, we could have calculated SS_{error} by working out an SS for each group separately and adding them up:

$$\begin{aligned} SS_{group1} &= \sum (x_1 - \bar{x}_1)^2 \\ SS_{group2} &= \sum (x_2 - \bar{x}_2)^2 \\ &\vdots \\ &\vdots \\ SS_{error} &= SS_{group1} + SS_{group2} + \dots + SS_{group5} \end{aligned}$$

Both approaches give the same answer.

III.6.5 Degrees of freedom:

If there are N observations in total, $df_{total} = N - 1$. If there are a treatments, $df_{treatment} = a - 1$. We can calculate the degrees of freedom for error like this:

$$df_{error} = df_{total} - df_{treatment} \quad (\text{Equ. III.29})$$

Alternatively, we could calculate df_{error} as the sum of the degrees of freedom within each treatment; if there are n observations in each of a treatments, there are $n - 1$ degrees of freedom within each treatment, and so $df_{error} = a(n - 1)$. This gives the same answer (since $df_{total} - df_{treatment} = [N - 1] - [a - 1] = [na - 1] - [a - 1] = na - a = a [n - 1]$). [44]

III.6.6 Mean squares:

Mean squares are easy; just divide each SS by the corresponding number of df . [44]

III.6.7 The F test:

The test statistic is the ratio $F = \text{MSTr}/\text{MSE}$. F is a ratio of two estimators of σ^2 the numerator (the between-samples estimator), MSTr , is unbiased when H_0 is true but tends to overestimate σ^2 when H_0 is false, whereas the denominator (the within samples estimator), MSE , is unbiased regardless of the status of H_0 . Thus if H_0 is true the F ratio should be reasonably close to 1, but if the μ_i 's differ considerably from each other, F should greatly exceed 1. Thus a value of F considerably exceeding 1 argues for rejection of H_0 .

$$F = \frac{MS_{\text{treatment}}}{MS_{\text{error}}} \quad (\text{Equ. III.30})$$

and it is distributed as $F_{\alpha-1, a(n-1)}$ — that is, as $F_{\text{treatment } df, \text{error } df}$, under the null hypothesis. So we can look up critical value of F in tables. If it's 'significant' (unlikely given the null hypothesis), we reject the null hypothesis and say that the treatment did influence our dependent variable.

Figure III.4 shows an F density curve and corresponding upper-tail critical value F_{α, ν_1, ν_2} . [39]

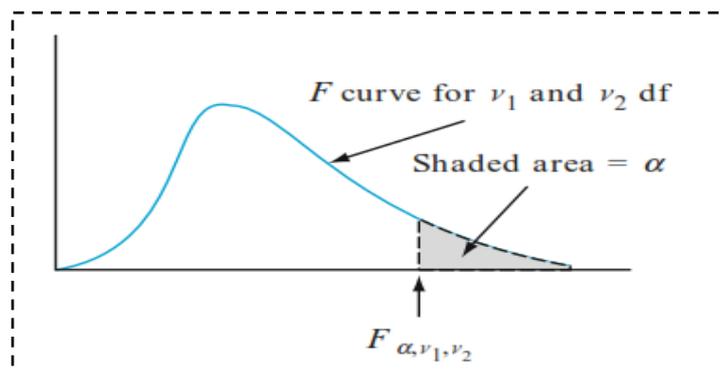


Fig. III.4 An F curve and critical value F_{α, ν_1, ν_2}

where: ν_1 is a numerator df , ν_2 denominator df , and α ; a shaded area.

III.6.8 ANOVA summary table:

ANOVA results are presented in a summary table (III.1) like this:

Source	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>
Treatment	$a-1$	$SS_{\text{treatment}}$	$SS_{\text{treatment}}/df_{\text{treatment}}$	$MS_{\text{treatment}}/MS_{\text{error}}$
Error(S/treatments)	$n(n-1)$	SS_{error}	$SS_{\text{error}}/df_{\text{error}}$	
Total	$N-1= an - 1$	SS_{total}	$SS_{\text{total}}/df_{\text{total}} [= s^2]$	

Tab. III.1 ANOVA summary table. [44]

III.7 Regression ANOVA: the other way to understand the basic logic

The splitting of the total sum of squares $\sum(Y_i - \bar{Y})^2$ into a part SSE, which measures unexplained variation, and a part SSR, which measures variation explained by the linear relationship, is strongly reminiscent of one-way ANOVA.

In fact, the null hypothesis $H_0: \beta_1 = 0$ can be tested against $H_a: \beta_1 \neq 0$ by constructing an ANOVA table (III.2) and rejecting H_0 if $f \geq F_{\alpha,1,n-2}$.

Source of variation	<i>df</i>	Sum of squares	Mean square	<i>F</i>
Regression	1	SSR	SSR	$\frac{SSR}{SSE/(n-2)}$
Error	$n-2$	SSE	$s^2 = \frac{SSE}{n-2}$	
Total	$n-1$	SST		

Tab. III.2 ANOVA table for simple linear regression. [39]

The *F* test gives exactly the same result as the model utility *t* test because $t^2 = f$ and $t_{\alpha/2,n-2}^2 = F_{\alpha,1,n-2}$. Virtually all computer packages that have regression options include such an ANOVA table in the output. [39]

III.8 Conclusion:

The methods presented in this chapter based on numerical analysis with Runge-Kutta 4, it's mathematical solutions to study the approximation's solutions of ordinary differential equations, also based on linear regression with least square method that gives the best fitted line and last but not least based on statistical study using the analysis of variance "ANOVA".

We will apply all this in the last chapter and show the results obtained.

CHAPTER IV

Conception & Results

IV.1 Introduction:

In this chapter, we translate non linear model to linear one by use numerical analysis with “*Runge-Kutta 4 (RK4)*” where the step size H is working to increase the lighting of the image compared with the original picture.

The new data (normal & pathological images) obtained from this method is going to use it to pass to the statistical study for *linear regression* then for “*ANOVA*” technique by use statistical test of *ANOVA* to detect the tumors of *MRI* images.

IV.2 Computer Identification:

- ✓ Manufacturer: DELL
- ✓ Model: INSPIRON N4050
- ✓ Processor: Intel(R) Core(TM) i5-2450M CPU @ 2.50Ghz 2.50Ghz
- ✓ Graphics Card: Intel(R) HD Graphics 3000
- ✓ Installed Memory (RAM): 6.00 GB
- ✓ Windows Edition: Windows 7
- ✓ System Type: 32-bit operating system
- ✓ Software: Matlab7.11.0 (R2010b)

IV.3 What is Matlab?

The name *MATLAB* stands for **MAT**rix **LAB**oratory. MATLAB was written originally to provide easy access to matrix software developed by the LINPACK (linear system package) and EISPACK (Eigen system package) projects.

MATLAB is a high-performance language for technical computing. It integrates computation, visualization, and programming environment. Furthermore, MATLAB is a modern programming language environment: it has sophisticated data structures, contains built-in editing and debugging tools, and supports object-oriented programming. These factors make MATLAB an excellent tool for teaching and research.

MATLAB has many advantages compared to conventional computer languages (e.g., C, FORTRAN) for solving technical problems. MATLAB is an interactive system whose basic data element is an array that does not require dimensioning. The software package has been commercially available since 1984 and is now considered as a standard tool at most universities and industries worldwide.

It has powerful built-in routines that enable a very wide variety of computations. It also has easy to use graphics commands that make the visualization of results immediately available. Specific applications are collected in packages referred to as toolbox. There are toolboxes for signal processing, symbolic computation, control theory, simulation, optimization, and several other fields of applied science and engineering.

IV.4 Magnetic resonance imaging (*MRI*):

Magnetic resonance imaging (*MRI*) is a medical imaging technique used in radiology to investigate the anatomy and function of the body in both health and disease. *MRI* scanners use strong magnetic fields and radio waves to form images of the body. The technique is widely used in hospitals for medical diagnosis, staging of disease and for follow-up without exposure to ionizing radiation.

➤ ***MRI* scan facts**

- ✓ *MRI* scanning uses magnetism, radio waves, and a computer to produce images of body structures.
- ✓ *MRI* scanning is painless and does not involve x-ray radiation.
- ✓ Patients with heart pacemakers, metal implants, or metal chips or clips in or around the eyes cannot be scanned with *MRI* because of the effect of the magnet.
- ✓ Claustrophobic sensation can occur with *MRI* scanning.

➤ **What is an *MRI* scan?**

An *MRI* (or magnetic resonance imaging) scan is a radiology technique that uses magnetism, radio waves, and a computer to produce images of body structures. The *MRI* scanner is a tube surrounded by a giant circular magnet. The patient is placed on a moveable bed that is inserted into the magnet. The magnet creates a strong magnetic field that aligns the protons of hydrogen atoms, which are then exposed to a beam of radio waves. This spins the various protons of the body, and they produce a faint signal that is detected by the receiver portion of the *MRI* scanner. The receiver information is processed by a computer, and an image is produced.

The image and resolution produced by *MRI* is quite detailed and can detect tiny changes of structures within the body. For some procedures, contrast agents, such as gadolinium, are used to increase the accuracy of the images.

➤ **When are *MRI* scans used?**

An *MRI* scan can be used as an extremely accurate method of disease detection throughout the body and is most often used after the other testing fails to provide sufficient information to confirm a patient's diagnosis. In the head, trauma to the brain can be seen as bleeding or swelling. Other abnormalities often found include brain aneurysms, stroke, tumors of the brain, as well as tumors or inflammation of the spine.

Neurosurgeons use an *MRI* scan not only in defining brain anatomy but in evaluating the integrity of the spinal cord after trauma. It is also used when considering problems associated with the vertebrae or inter vertebral discs of the spine. An *MRI* scan can evaluate the structure of the heart and aorta, where it can detect aneurysms or tears. *MRI* scans are not the first line of imaging test for these issues or in cases of trauma.

It provides valuable information on glands and organs within the abdomen, and accurate information about the structure of the joints, soft tissues, and bones of the body. Often, surgery can be deferred or more accurately directed after knowing the results of an *MRI* scan.

IV.5 EXPERIMENTAL RESULTS

IV.5.1 Global flow chart:

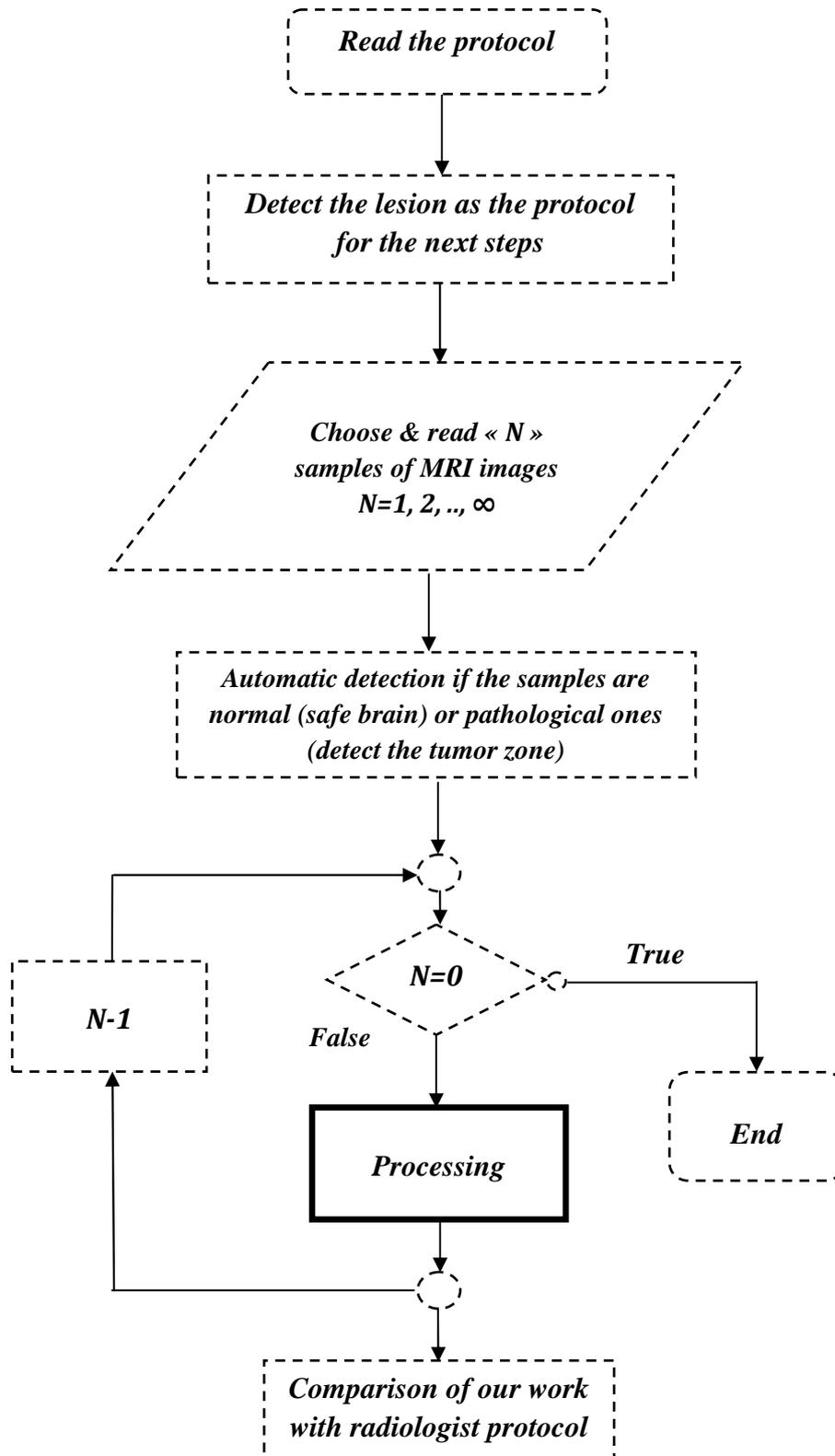


Fig. IV.1 Global flow chart

IV. 5.2 Analysis of flow chart:

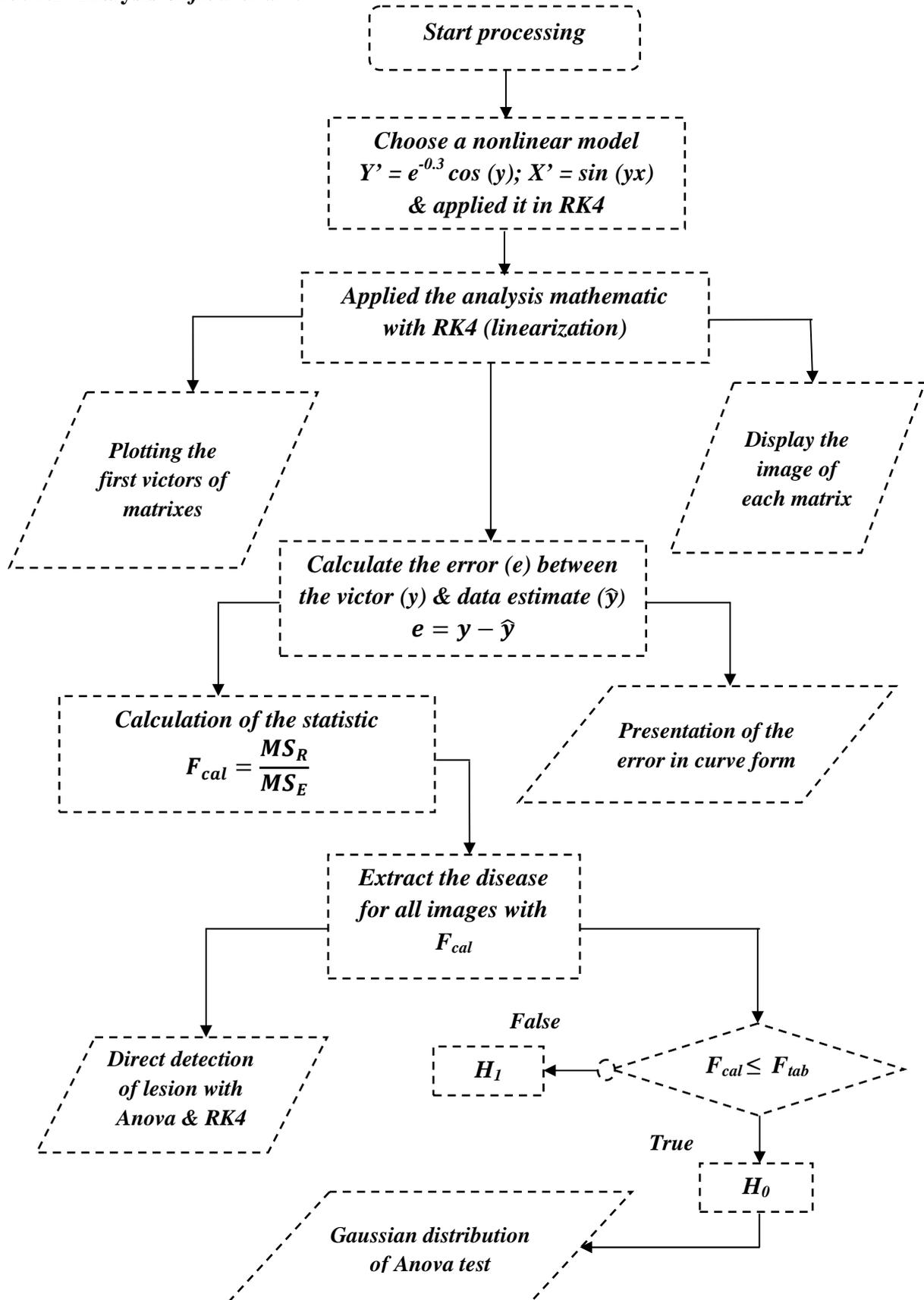


Fig. IV.2 Analysis of flow chart

IV.5.3 Analysis of data (the protocol radiologic):

Our protocol is for a patient aged 55 years; He made examination by *MRI* scan with injection of contrast medium. The machine used: type "SIEMENS", and with the field $B = 1.5$ Tesla. The sequences performed T1 and T2. The result *MRI* scans of a tumor appear in the middle of the field on the right side and the third ventricle is to evoke the tumor.

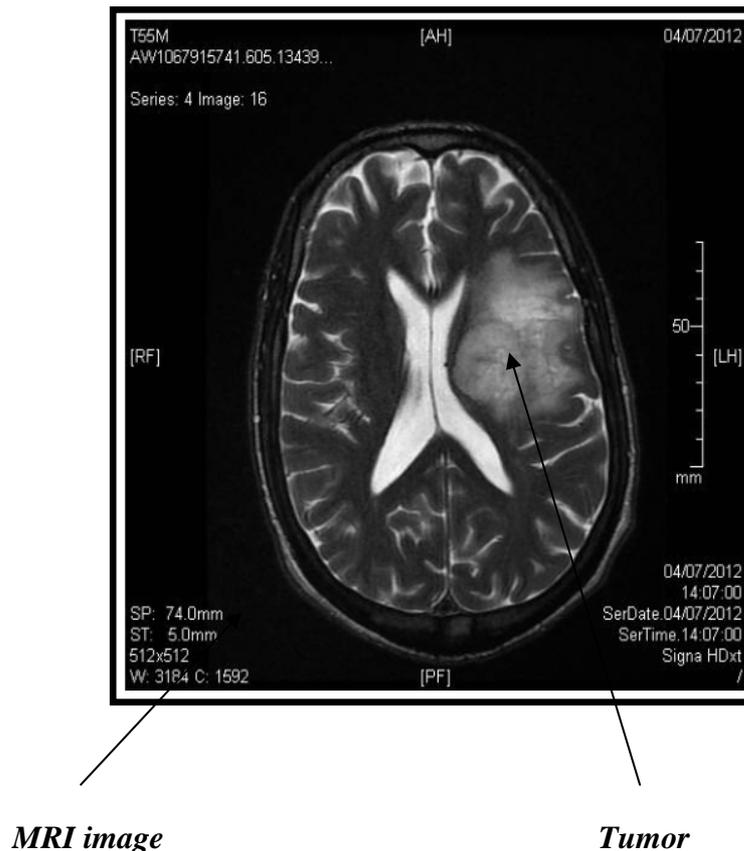


Fig. IV.3 MRI scan

IV.5.4 Choosing samples of *MRI* images (multi) with automatic detection:

First of all, we choose *multi* samples (unlimited number of it) of *MRI* image as shown in figure. IV.4 (a) and then *detect automatically* if these samples are normal (*safe brain*) or pathological ones (*detect the zone of tumor*), we have their all samples with *full length (size)*; figure. IV.4 (b). In the bottom of pathological images, we have zoom figure of detected zone of the tumor; see figure. IV.4 (c).

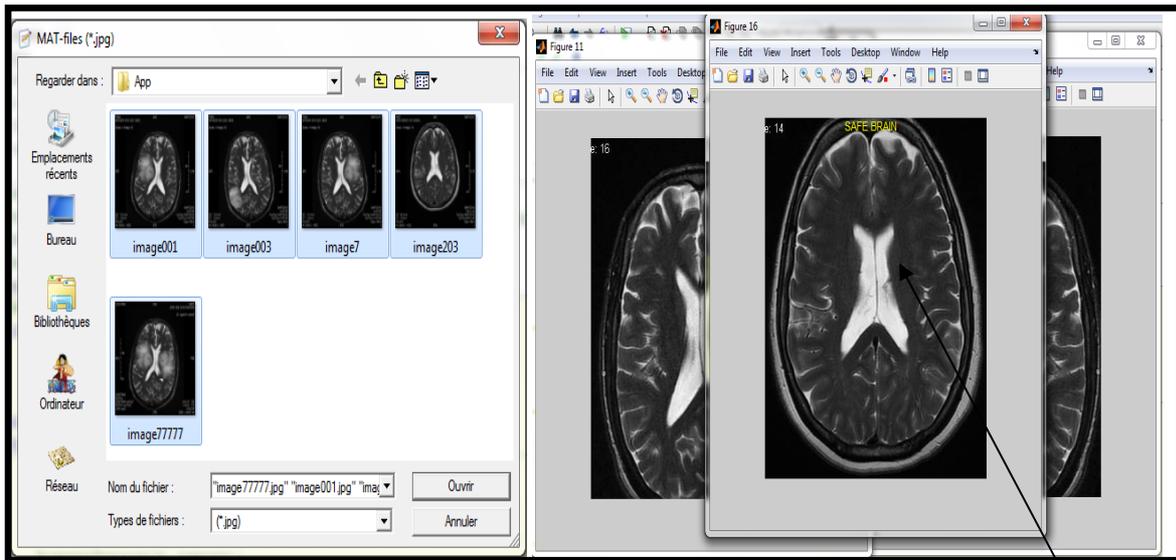


Fig. IV.4 (a) Selection of multi MRI images ; Sample of normal image (safe brain)

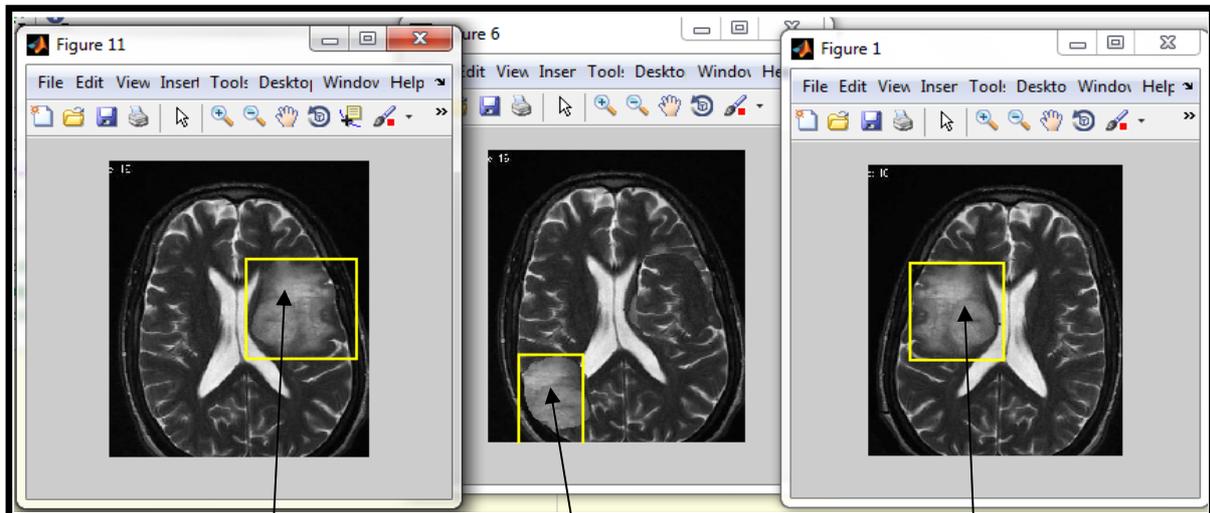


Fig. IV.4 (b) Samples of pathological images

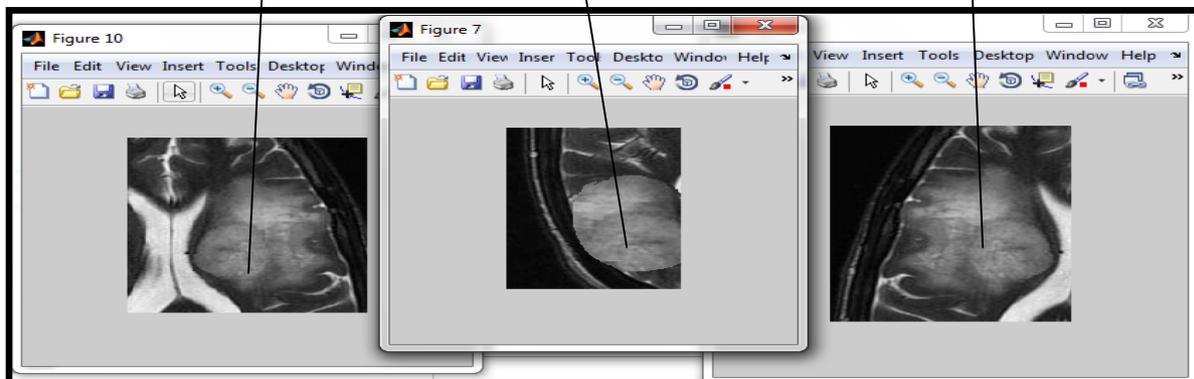


Fig. IV.4 (c) Zoom of tumors zone

Fig. IV.4 Choosing samples of images with automatic detection

- *Note:*

The following steps are applied to *every* single sample of *MRI* image that we selected, means the same process for each sample. Please note that the following results are for one single sample and it shown in the next titles.

IV.5.5 Analysis of RK4:

First of all, we choose a nonlinear model (in our work: $Y' = e^{-0.3} \cos(y)$) & $X' = \sin(xy)$ and applied it in *RK4*; see Fig. IV.5

```
f = inline('exp(-0.3*x)*cos(y)', 'x', 'y');
g = inline('sin(y*x)', 'x', 'y');
```

Fig. IV.5 Matlab code of nonlinear model: $f(t, x, y)$; $g(t, x, y)$

Second of all, we applied the analysis mathematic with *RK4* to do the *linearization* (translate nonlinear model to linear one), after that we choose the first vectors of matrixes of normal & pathological image, and then we display it in curves form by two ways: before & after used *RK4*. Fig.IV.6 shows all of that.

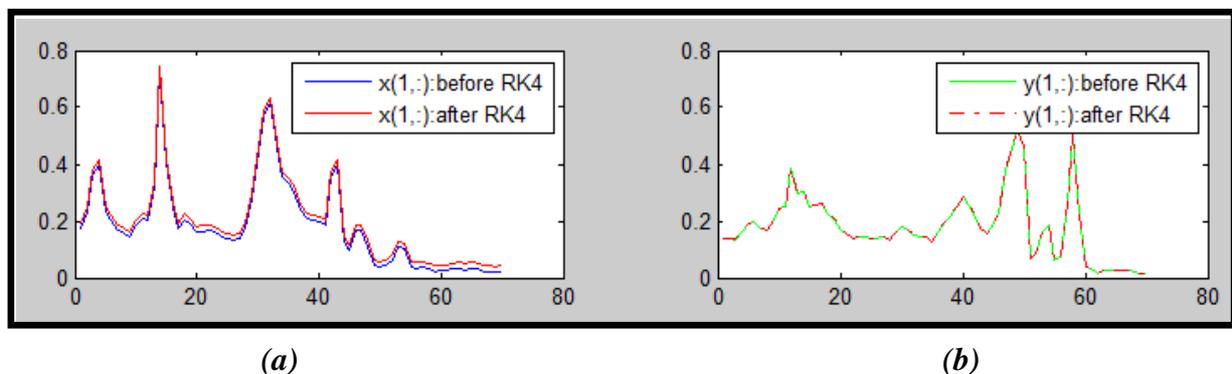


Fig. IV.6 Plotting the first vectors of matrixes (normal & pathological image)

(a) Curve of pathological image(x) before used *RK4* (blue color) & after *RK4* (red color).

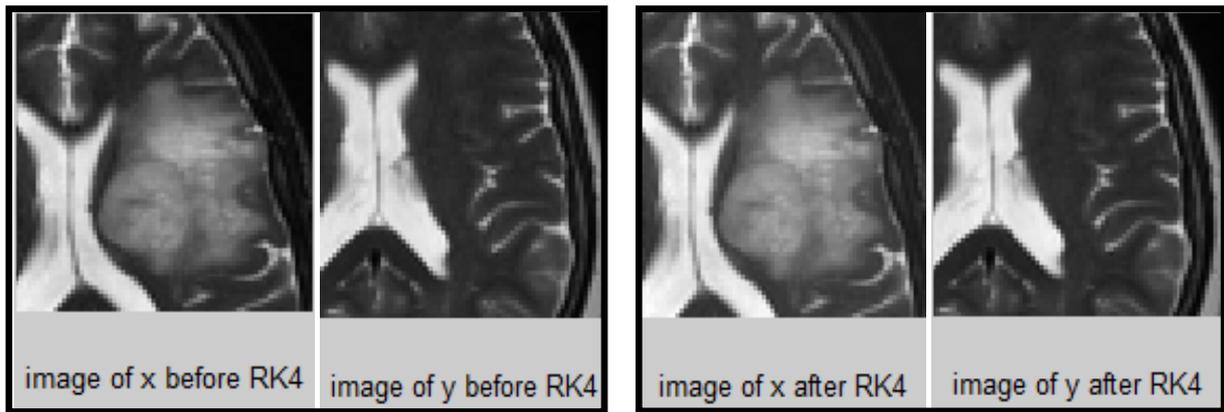
(b) Curve of normal image (y) before used *RK4* (green color) & after used *RK4* (red color).

Figure IV (6.a) shows us two curves of the image (x) where blue is located down the red .The second figure (6.b) shows the color green beneath red varying small. All those curves red Accomplished with *RK4*.

- *Note:*

The presence of the red curve in pathological image (x) explains why the image appears after **RK4** more Lighting in front of normal image (y).

And last but not least, we display the image for each matrix by two ways either: before & after used **RK4**, like we displayed in the precedent figure curves of vectors (x & y) and now we will show images of these matrixes for the step size (**H=0.07**) which became more lighting as presented in figure IV.7



(a)

(b)

Fig. IV.7 Display the image for each matrix by two ways (before & after used **RK4**)

where: (a) The grayscale luminosity before used **RK4** & (b) After used **RK4** for step size **H=0.07**.

- *Note :*

Whenever we have increased **H** we get more Lighting picture and result obtained to be bad as in fig. IV(8.a) ,where **H = 0.7**, haven't detect any tumors & it presented only white picture. See fig. IV(8.b)



(a)

(b)

Fig. IV.8 Presentation of image after used **RK4** with variation of the step size **H**

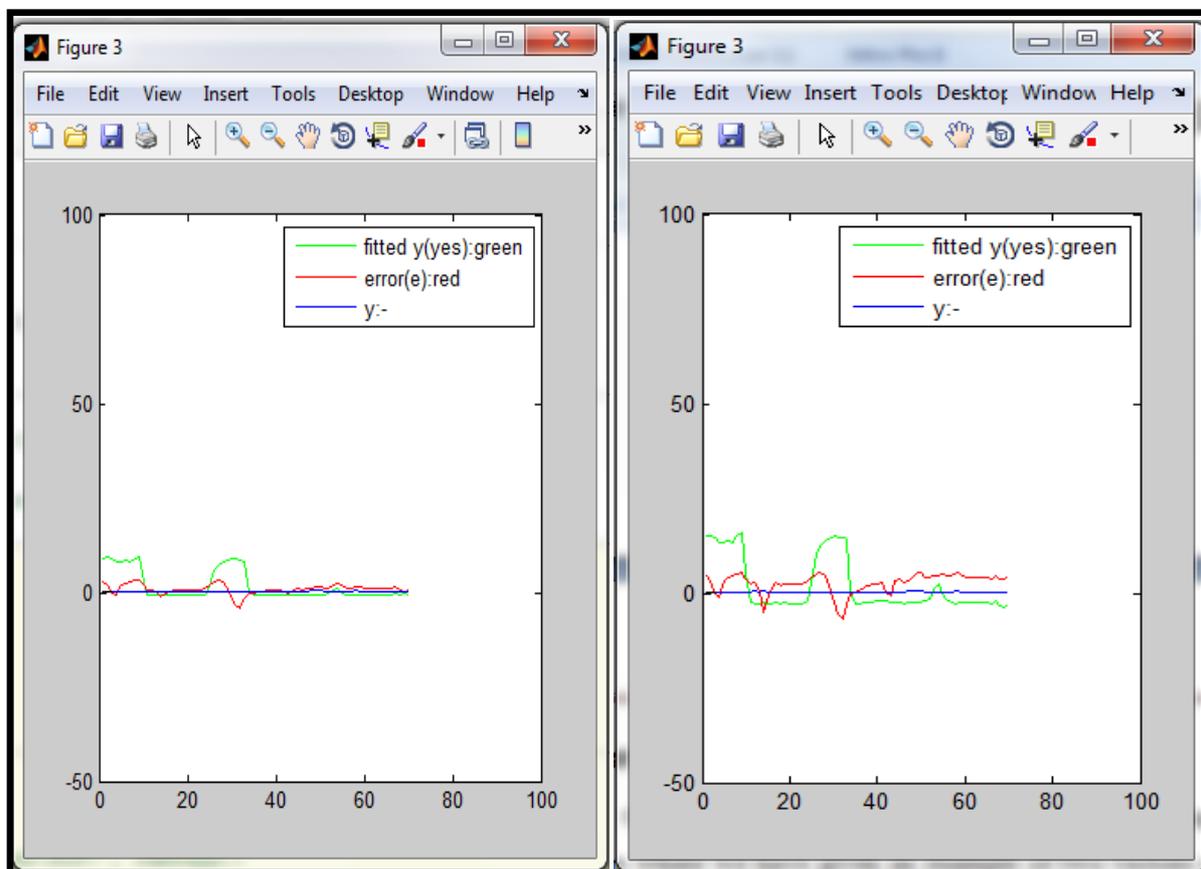
where: (a). The grayscale luminosity after used **RK4** for H increase ($H=0.7$) &
 (b). No detection of lesion

IV.5.6 Calculation of the error between “y” and fitted regression line:

After use **RK4**, we pass to calculate the error between fitted vector of y and y of image obtained (full size), as in follow equation where we have given an example of two vectors of the both images and detect the lesion or the error by calculate the error for one vector.

$$e = y - \hat{y} \quad (\text{Equ.IV.1})$$

where: y is the vector, & \hat{y} is data estimate. See figure. IV.9



(a)

(b)

Fig. IV.9 Presentation of the error e , y & \hat{y} for both curves

where: a. Curve for $H=0.07$; b. Curve for $H=0.7$

We note that the error rate in the figure(9.a) lower than in figure (9.b) and this is what explains and confirms the role of step size H in the control of picture, this is what explains the success of our method and its impact in the discovery of tumors.

IV.5.7 Calculation of the statistic:

After previous studies we are going to discover tumors through the use of an equation of Anova (Equ. IV.2);

$$F_{cal} = \frac{MS_R}{MS_E} \tag{Equ. IV.2}$$

where: MS_R is the within-groups variation; & MS_E is the between-groups.

We extract the disease for all images with calculate F_{cal} by two ways: directly on the pathological image and from distribution of Anova test: See fig. IV.10

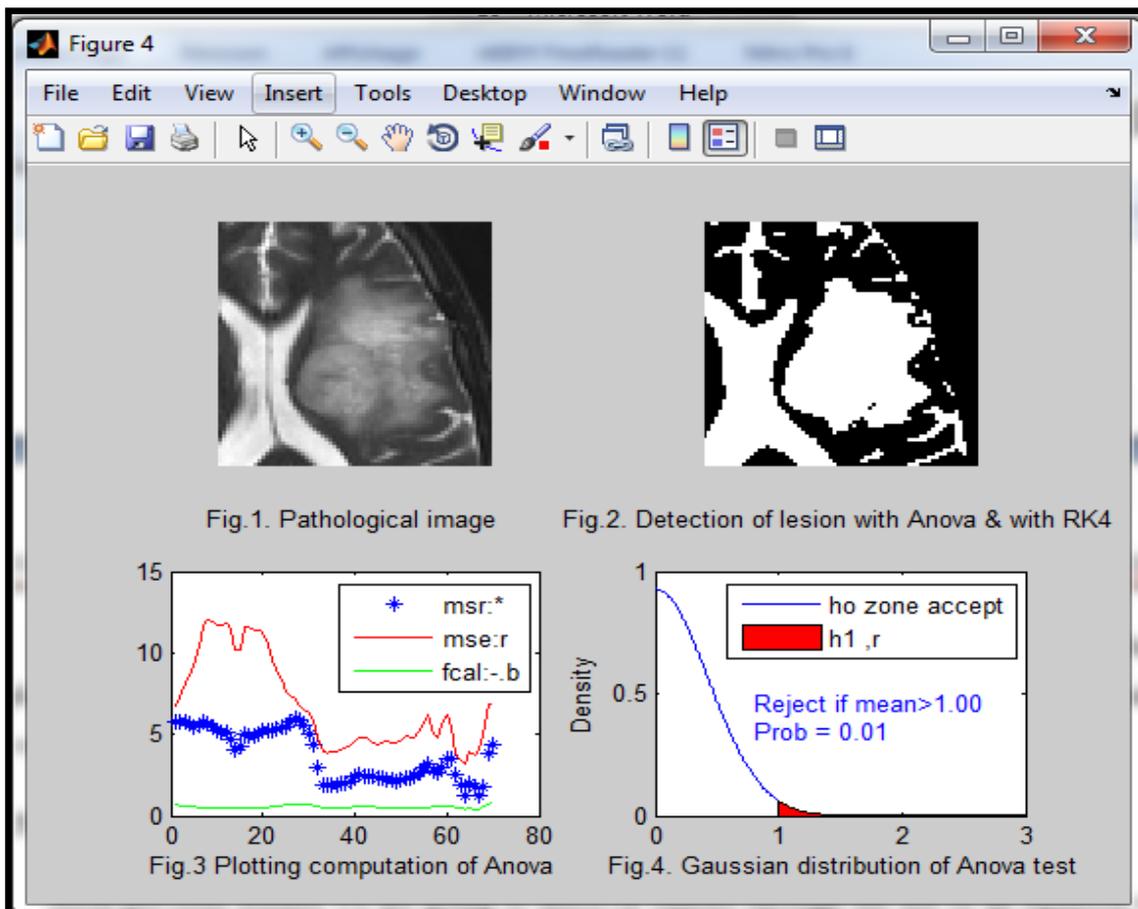


Fig. IV.10 Detect the lesion with two ways

From figure IV.10 the first image in the top left (Fig.1) is the pathological image. The next image in the top right (Fig.2) right is the detection of lesion directly on the pathological image, which present with white color. The next figure (bottom left “Fig.3”) is plotting the computation of Anova technique, where “Fig.3” shows: F_{cal} (green color) its value beside zeros number, MS_R (blue stars) color & MS_E (red color). For the last figure (bottom right “Fig.4”) which present present gauss curve (gaussian distribution of Anova test), and from the table of Anova (fisher table) test we have:

for $\alpha = 0.01$:

*Degree of freedom: df :

* $\nu = n-1$.

* $F_{tab} = 1$.

*Hypothesis H_0 will be:

$$\begin{cases} \text{If } F_{cal} \leq F_{tab} \Rightarrow f_{test} \text{ with (Anova)} \rightarrow \text{accept } H_0 \\ \text{If } F_{cal} > F_{tab} \Rightarrow f_{test} \text{ reject } H_0. \text{ (red color)} \end{cases}$$

IV.5.8 Comparison between Anova with *RK4* and without it:

The result with *RK4* (nonlinear model) presented in fig IV.11 (a), is more precise and accurate than Anova without it (linear model) as in fig. IV.11 (b), because with *Runge-kutta 4* we have the step size H which that control step to show the image resolution.

The best result is for H minimal and here hence shows the superiority of our idea of using *RK4*.

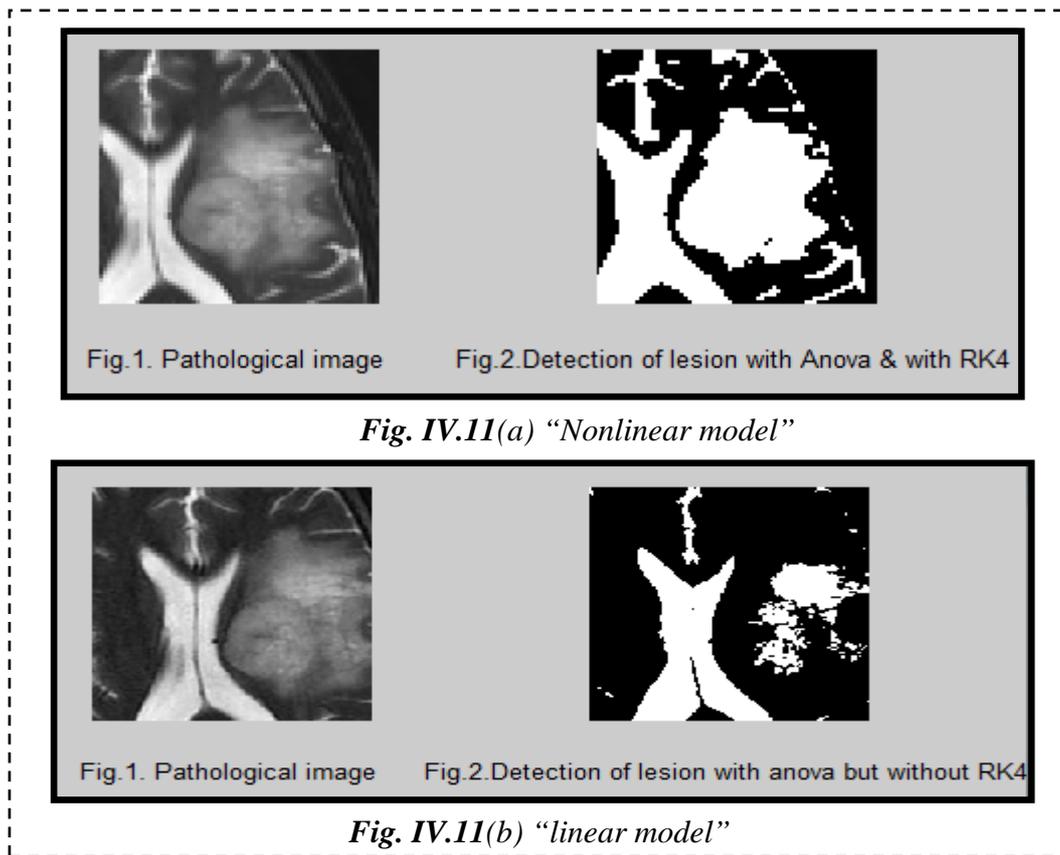


Fig. IV.11 Comparison between nonlinear model & linear one

IV.6 What makes our work special than others done before? (Comparison)

1. (a) Sample of MRI image with surface 200 (X work) → (b) Sample of full MRI images (our work):

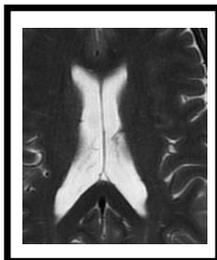


Fig. IV.12 (a)

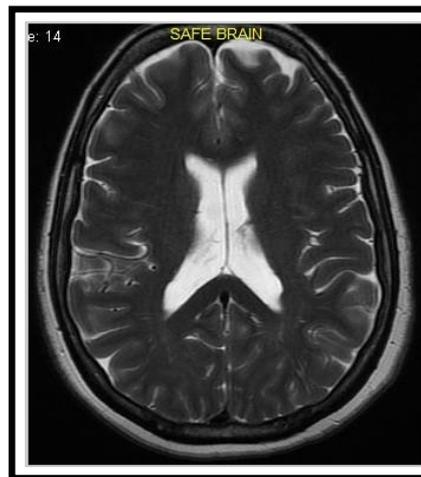


Fig. IV.12 (b)

Fig. IV.12 Comparison ("length of image")

where: (a) is a sample of MRI image with *length of 200*. & (b) is a sample of *full MRI image*.

2. (a) *Single MRI image (X work)* → (b) *Multi MRI image (our work)*:

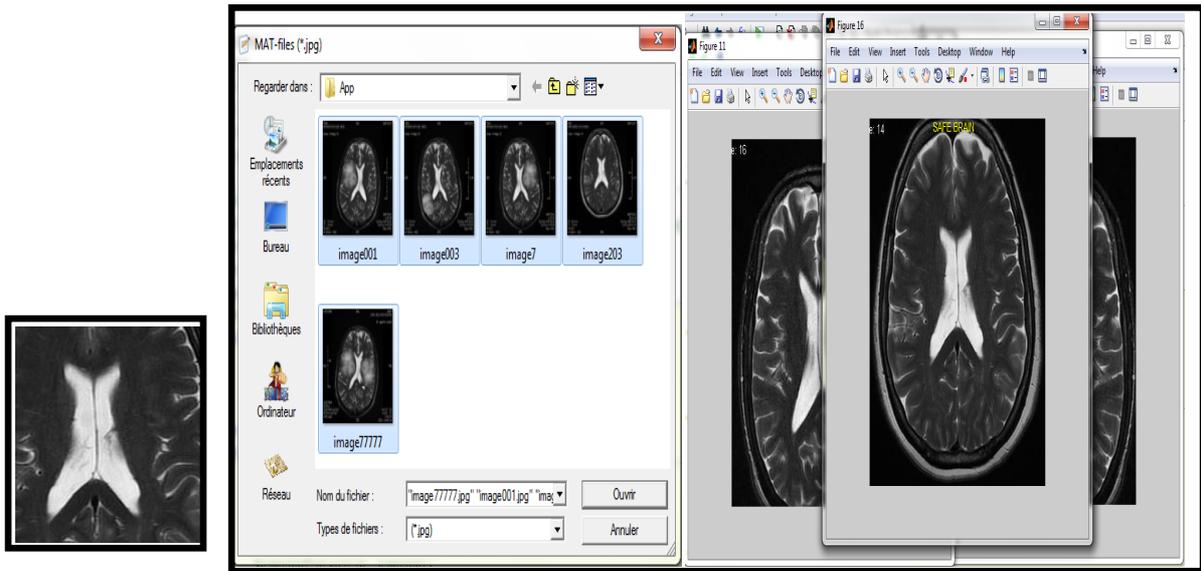


Fig. IV.13 (a)

Fig. IV.13 (b)

where: (a) is *single* sample of *MRI* image. & (b) is selection of *multi* samples of *MRI* images.

Fig. IV.13 Comparison (“number of image”)

3. (a) *No detection of tumor zone (X work)* → (b) *Automatic detection of tumor zone (our work)*:

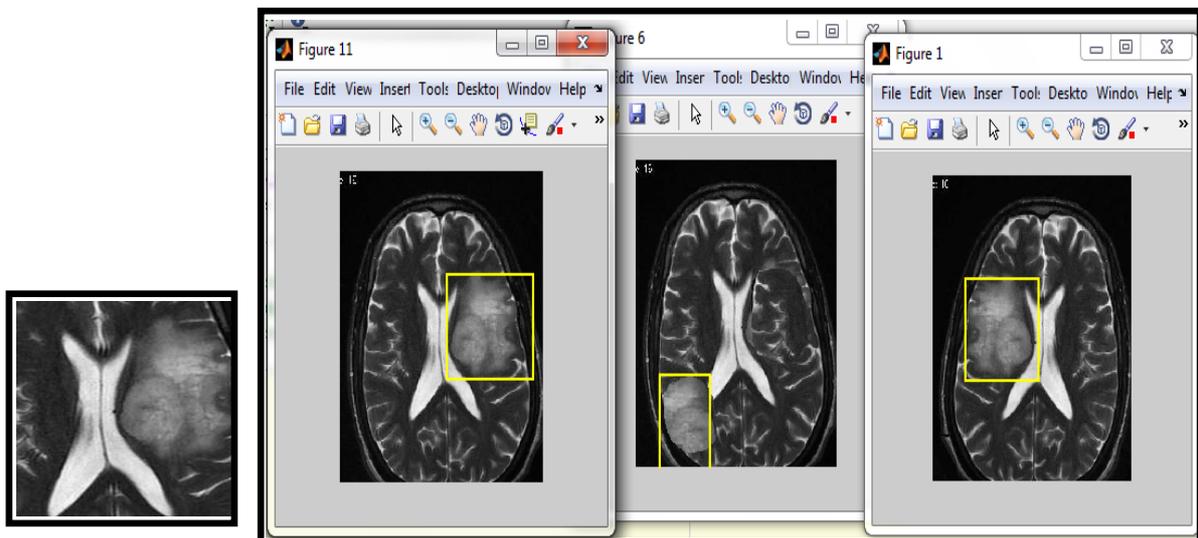


Fig. IV.14 (a)

Fig. IV.14 (b)

Fig. IV.14 Comparison (“detection of tumor zone”)

where: (a) is *MRI* image without detection of the tumor zone. & (b) is *MRI* image with automatic detection of the tumor zone.

4. Execution time optimization:

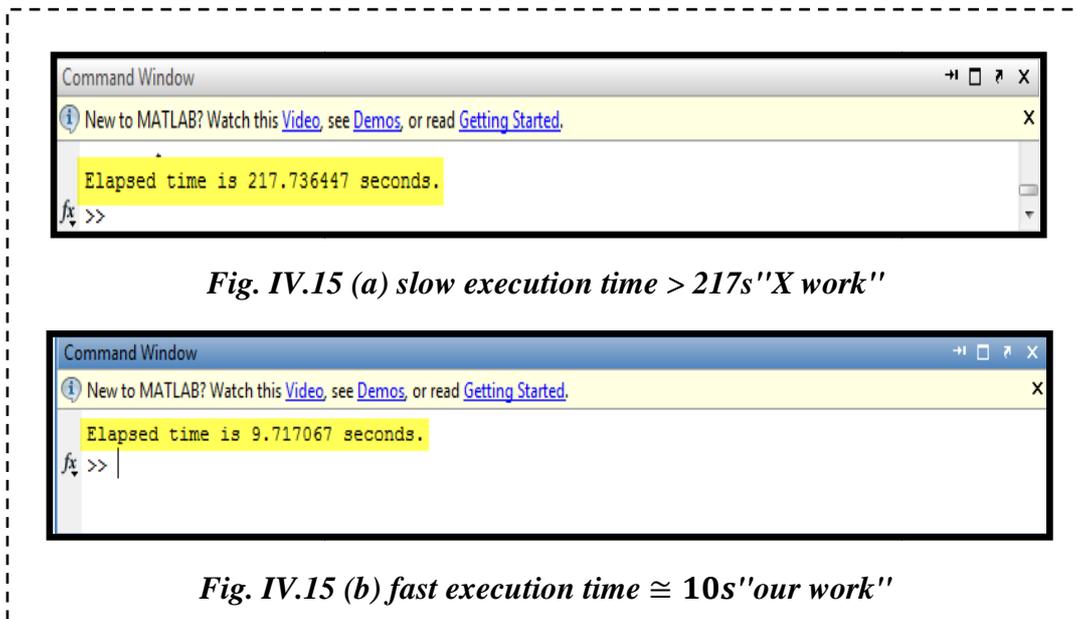


Fig. IV.15 (a) slow execution time > 217s''X work''

Fig. IV.15 (b) fast execution time \cong 10s''our work''

Fig. IV.15 Comparison ("execution time")

- **Note:** these 10s are the timing of selection of *MRI* samples, *plus* the execution time; which means that the real execution time is less than 10s.

5. Interface system (well organized):

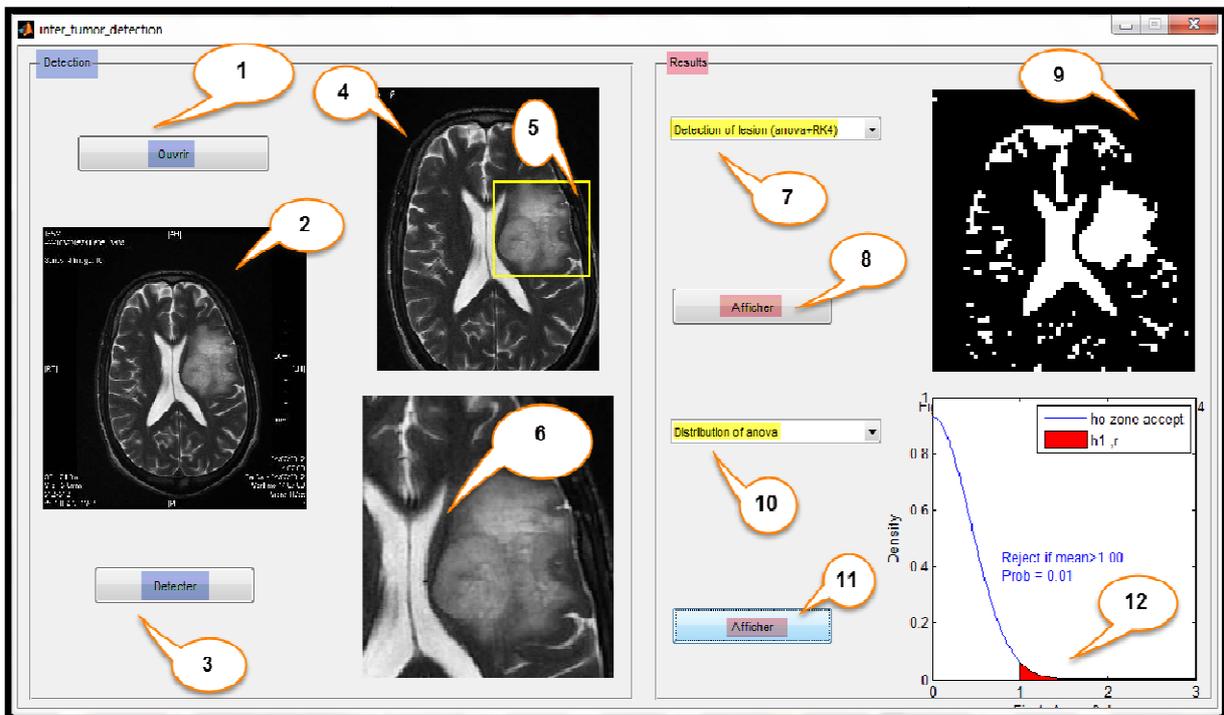


Fig. IV.16 (a) Interface system for MRI sample with tumor on the right side

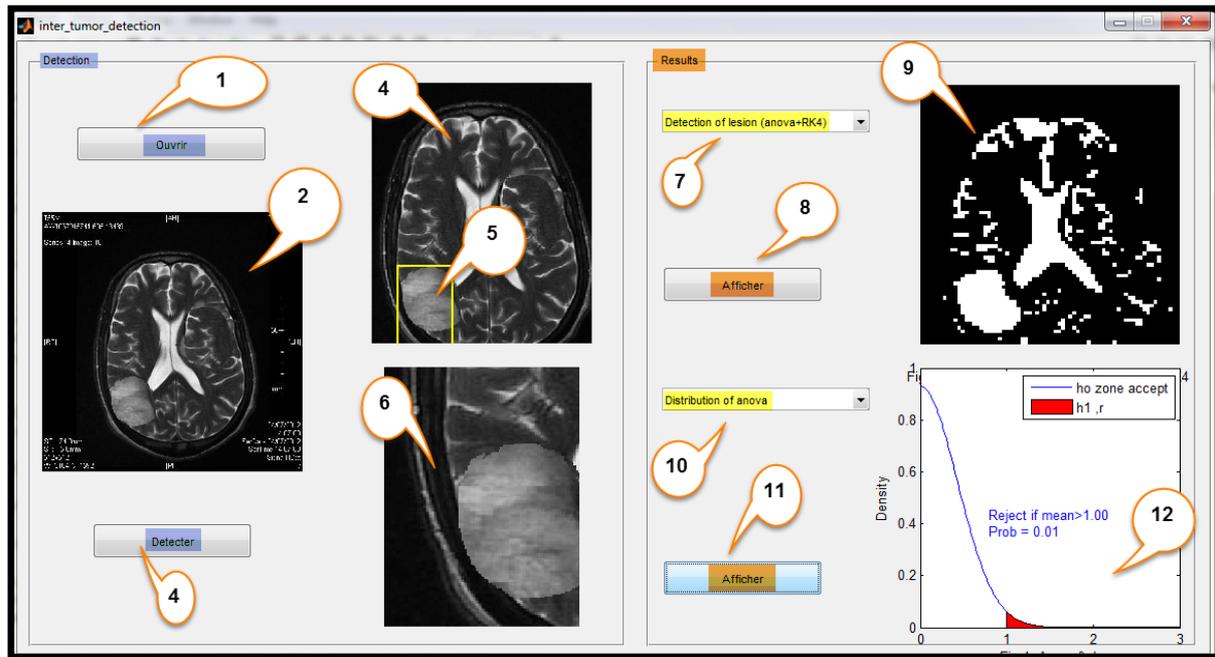


Fig. IV.16 (b) Interface system for different MRI sample with tumor on the left side

Fig. IV.16 Interface system

where:

1. Selection button of MRI samples ; 2. MRI scan
3. Execution button of detection if where the samples are normal (safe brain) or pathological ones (detection of the tumor zone)
4. Full MRI image (pathological one) ; 5. Detection of tumor zone (Automatic)
6. Zoom of tumor zone ; 7. Selection of display types of RK4 applications
8. Execution button of numerical applications (RK4) ; 9. Detection of lesion with RK4
10. Selection of display types of ANOVA applications
11. Execution button of statistical applications (ANOVA) ; 12. Distribution of ANOVA test

- **The following table (IV.1) summarizes all the interesting points that we have mentioned above:**

	<i>Our "ANOVA" project</i>	<i>Previous projects of ANOVA</i>
<i>MRI sample</i>	<i>Multi</i>	<i>Single</i>
<i>Surface</i>	<i>Full (512x512)</i>	$\leq 200 \times 200$
<i>Tumor zone detection</i>	<i>Auto</i>	×
<i>Execution time</i>	<i>Fast ($\approx 10s$)</i>	<i>Slow (almost 5min)</i>
<i>Interface.sys organization</i>	✓	×
<i>Results</i>	<i>Good (Fig. IV.11a)</i>	<i>Poor (Fig. IV.11b)</i>

Tab. IV.1 Comparison between our & previous ANOVA projects

IV.7 Conclusion:

From this study we can distinct:

- Statistical methods used to compare between new & old models in different specialties as (chemic, architect, processing of image, pharmacology...).
- Our study is applied for *Multi* samples of *MRI* image.
- *RK4* is one of ideas to translate from a nonlinear model to linear one from the step size *h*.
- The step size *h* used to command the image from increased or decreased the lighting.
- If $h < 0.4$ the image display different steps of black, if $h > 0.5$, the image will be whiter until 0.7 where it can't detect the lesion.
- The error will be minimal for $0 < h < 0.1$, which means the image approximate to original picture.
- The statistical study is used to do the comparison between two models: a linear & nonlinear model.
- To detect the lesion for non linear model is more precise & extract excellent result in front of applied a linear model.
- *ANOVA* technique proves that can be used for full & multi *MRI* images.
- We have add a new work in front of the article published [4][5][4] or precedent memories which detected the lesion for *MRI* multi images & in short time (*before*, the execution time is *almost 5min*, and *now is less than 10 seconds*).

Conclusion & Perspectives

From this work we conclude the following:

- There are two types of images, *analog* and *digital*; both are used in *medical imaging*.
- Analog images are the type of images that we, as humans, look at. They include such things as photographs, paintings, TV images, and all of our medical images recorded on film or displayed on various display devices, like computer monitors.
- The advantage of digital images is that they can be processed, in many ways, by computer systems:
 - ✓ Image reconstruction (CT, MRI, SPECT, PET, etc).
 - ✓ Image reformatting (Multi-plane, multi-view reconstructions).
 - ✓ Wide (dynamic) range image data acquisition (CT, digital radiography, etc).
 - ✓ Image processing (to change contrast and other quality characteristics).
 - ✓ Fast image storage and retrieval.
 - ✓ Fast and high-quality image distribution (teleradiology).
 - ✓ Controlled viewing (windowing, zooming, etc).
 - ✓ Image analysis (measurements, calculation of various parameters, computer aided diagnosis, etc).
- Image compression is the process of reducing the numerical size of digital images.
- *Lossless* compression is when there is no loss of image quality, and is commonly used in many medical applications.
- *Loss* compression results in some loss of image quality and must be used with care for diagnostic images.
- There are two types of medical imaging modalities:
 - ✓ Modalities use *ionizing radiation* (Radiography, Fluoroscopy, CT scanner and Mammography), this type of radiation can causing *serious damage* to the body and to its genetic material.
 - ✓ Modalities use *non-ionizing radiation* Examples of such radiation are ultrasound (US), i.e. high-frequency sound, and radio frequency waves are magnetic resonance image (MRI). This type of radiation does not have the potential to damage the body directly and the risks associated with its use are considered to be *very low*.

Conclusion & Perspective

- Detect the lesion with **RK4** is new idea with an excellent results.
- Statistical methods used to compare between new & old models in different specialties as (chemic, architect, processing of image, pharmacology...).
- Our study is applied for **Multi** samples of **MRI** image.
- **RK4** is one of ideas to translate from a nonlinear model to linear one from the step size **h**.
- The step size **h** used to command the image from increased or decreased the lighting.
- If **h** < 0.4 the image display different steps of black, if **h** > 0.5, the image will be whiter until 0.7 where it can't detect the lesion.
- The error will be minimal for $0 < h < 0.1$, which means the image approximate to original picture.
- The statistical study is used to do the comparison between two models: a linear & nonlinear model.
- To detect the lesion for non linear model is more precise & extract excellent result in front of applied a linear model.
- **ANOVA** technique proves that can be used for full & multi **MRI** images.
- We have add a new work in front of the article published [4][5][45] or precedent memories which detected the lesion for **MRI** multi images & in short time (we have optimized the execution time from **almost 5min** to **less than 10 seconds**.)

In the last, we propose using as perspective the **Artificial Neural Networks (ANN)** technique with **RK4** for **multi** MRI images.

Bibliographies

[1]: http://en.wikipedia.org/wiki/Digital_imaging, 14/05/2014, 20:38.

[2]: Roger_Bourne, Fundamentals of Digital Imaging in Medicine, Springer-Verlag ©London Limited 2010.

[3]: Chris Guy, Dominic ffytche, An introduction to the principles of medical imaging, Copyright © 2005 by Imperial College Press.

[4]: K.el kourd, "Detect the Tumor with Numerical Analysis and With "ANOVA" Technique for MRI Image", International Journal of Engineering and Innovative Technology (IJEIT), Volume 3, Issue 1, July 2013, ISSN: 2277-3754 ISO 9001:2008 Certified, Florida, pp:257-260, impact factor. 1.895

[5]: K.el kourd , " Linearization of exponential model to extract the lesion from pathological image of MRI with two techniques STUDENT & FISHER",Computer Applications &Technology,(ICAAAT),july , ,2012, pp:39-43.

[6]: Jayaraman, S.Esakkirajan, T.Veerakumar, Digital Image Processing, ©2009 by Tata McGraw Hill Education Private Limited.

[7]: G. Dougherty, Digital Image Processing for Medical Applications, ©2009.

[8]: Al Bovik, Handbook of image and video processing, © Copyright 2000 by Academic Press.

[9]: Rafael_C._Gonzalez,_Richard_E._Woods, Digital Image processing, © 2002 by Prentice-Hall, Inc.

[10]: Taylor & Francis, Digital Image processing, © 2011 by Group, LLC.

[11]: Oleg S. Pinykh, Digital Imaging and Communications in Medicine (DICOM), ©2012 by Springer-Verlag Berlin Heidelberg.

Bibliographies

[12]: Abhishak Yadav, Poonam Yadav, Digital image processing, Copyright © 2009 by Laxmi Publications Pvt. Ltd.

[13]: Dowsett et al, Copyright © 2006, p. 76. Reproduced by permission of Edward Arnold (Publishers) Ltd.

[14]: Copyright © Wolbarst(1993), p. 16.

[15]: R. Nick Bryan, Introduction to the Science of Medical Imaging, © Cambridge University Press 2010.

[16]: Michael. Y. M. Chen et al, Access Medicine, Copyright © 2004 by the McGraw-Hill Companies, Inc.

[17]: Anthony B. Wolbarst, Patrizio Capasso, Andrew R. Wyant, Medical Imaging: Essentials for Physicians, Copyright © 2013 by John Wiley & Sons, Inc.

[18]: ISAAC N. BANKMAN, Medical Imaging, Copyright © 2000 by Academic press.

[19]: <http://www.radiologyassistant.nl/en/p47a585a7401a9/breast-mri.html>, 14/03/2014, 3:28

[20]: JOHN L. SEMMLOW, Biosignal and Biomedical Image Processing, © Copyright 2004 by Marcel Dekker, Inc. All Rights Reserved.

[21]: Vorgelegt von, Medical Image Processing, © Copyright 2008,2009, Copyright Frank Enders All Rights Reserved.

[22]: http://en.wikipedia.org/wiki/Magnetic_resonance_imaging, 05/05/2014, 22:19.

[23]: http://psychcentral.com/lib/what-is-functional-magnetic-resonance-imaging_fmri/0001056, 08/05/2014, 19:43.

[24]: Gear, C.W. 1971, Numerical Initial Value Problems in Ordinary Differential Equations (EnglewoodCliffs, NJ: Prentice-Hall).

[25]: Andrew Rutherford, Introducing anova and ancova a glm approach, Copyright © 2001.

[26]: Fisher, R.A. (1925), Statistical Methods for Research Workers. Oliver & Boyd.

Bibliographies

[27]: Rattenbury N, Almost Runge-Kutta methods for stiff and non-staiff problems, Ph.D Dissertation, The University of Auckland, New Zealand, 2005.

[28]: http://en.wikipedia.org/wiki/Ordinary_differential_equation, 30/04/2014, 00:55.

[29]: Ken Wong, Solving Ordinary Differential Equations With Runge-Kutta Methods, Copyright © Oct 2009.

[30]:<http://mathfaculty.fullerton.edu/mathews/n2003/Euler%27sMethodMod.html>, 05/05/2014, 14:03.

[31]: Butcher J. C., General linera methods: A survey, Appl Numer Math 1, 1985.

[32]: Butcher, J. C. and Wanner, G., Ruge-Kutta methods: some historical notes, Appl Numer Math 22, 1996.

[33]: Claus Bendtsen & Per Grove Thomsen, Numerical Solution of Differential Algebraic Equations, Copyright © IMM-REP-1999-8.

[34]:<https://www.calvin.edu/~scofield/courses/m231/materials/rungeKuttaFormulas.pdf>, 25/04/2014, 18:30

[35]:http://www.ddt.cs.vsu.ru/vlab380/obrazcy/Neumann_vl/runge_kutta.html, 25/04/2014, 19:36.

[36]: Ballistic of the Future, J. M. J. Kooy and J. W. H. Uytendogaart, McGraw-Hill Book Company, Inc. New York, 1946.

[37]:http://search.4shared-china.com/q/1/mws_gen_ode_txt_runge4th,13/04/2014, 22:29.

[38]: Miller, Rupert G, Beyond ANOVA, basics of applied statistics, Copyright © 1986 by John Wiley & Sons, Inc.

[39]: Jay L. Devore, Kenneth N. Berk, Modern Mathematical Statistics with Applications, © Springer Science + Business Media, LLC 2012.

[40]: <http://www.weibull.com/DOEWeb/introduction.htm1>, 2/6/2012, 15:45.

Bibliographies

[41]: Dominick Salvatore, Derrick Reagle, Statistics and econometrics, Copyright © 2002 by The McGraw-Hill Companies, Inc.

[42]:<http://www.economics.soton.ac.uk/staff/aldrich/fisherguide/nature.htm>, 05/05/2014, 16:37.

[43]:http://en.wikipedia.org/w/index.php?title=Factorial_ANOVA&redirect=no, 12/6/2012 at 15:00.

[44]: Rudolf N. Cardinal, ANOVA in practice and complex ANOVA designs, Version of May 2004.

[45]: K.el kourd, " The detection of disease by statistic test of "analyze of variance", Computer Applications & Technology , 20 Jan. 2013 , IEEEExplore, ISSN:978-1-4673-5284-0,pp:1-6

Annex

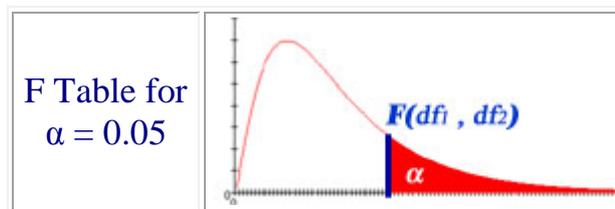
Table of critical values for the F distribution (for use with ANOVA):

How to use this table:

There are two tables here. The first one gives critical values of F at $\alpha = 0.05$ level of significance. The second table gives critical values of F at $\alpha = 0.01$ level of significance.

1. Obtain your F-ratio. This has (x, y) degrees of freedom associated with it.
2. Go along x columns, and down y rows. The point of intersection is your critical F-ratio.
3. If your obtained value of F is equal to or larger than this critical F-value, then your result is significant at that level of probability.

An example: I obtain an F ratio of 3.96 with (2, 24) degrees of freedom. I go along 2 columns and down 24 rows. The critical value of F is 3.40. My obtained F-ratio is larger than this, and so I conclude that my obtained F-ratio is likely to occur by chance with a $\alpha < .05$.



/	df ₁ =1	2	3	4	5	6	7	8	9	10	12	15	20	24	30	40	60	120	∞
d	16	19	21	22	23	23	23	23	24	24	24	24	24	24	25	25	25	25	25
f₂	1.4	9.5	5.7	4.5	0.1	3.9	6.7	8.8	0.5	1.8	3.9	5.9	8.0	9.0	0.0	1.1	2.1	3.2	4.3
=	47	00	07	83	61	86	68	82	43	81	06	49	13	51	95	43	95	52	14
1	6	0	3	2	9	0	4	7	3	7	0	9	1	8	1	2	7	9	4
2	18.	19.	19.	19.	19.	19.	19.	19.	19.	19.	19.	19.	19.	19.	19.	19.	19.	19.	19.
	51	00	16	24	29	32	35	37	38	39	41	42	44	45	46	47	47	48	49
	28	00	43	68	64	95	32	10	48	59	25	91	58	41	24	07	91	74	57
3	10.	9.5	9.2	9.1	9.0	8.9	8.8	8.8	8.8	8.7	8.7	8.7	8.6	8.6	8.6	8.5	8.5	8.5	8.5
	12	52	76	17	13	40	86	45	12	85	44	02	60	38	16	94	72	49	26
	80	1	6	2	5	6	7	2	3	5	6	9	2	5	6	4	0	4	4
4	7.7	6.9	6.5	6.3	6.2	6.1	6.0	6.0	5.9	5.9	5.9	5.8	5.8	5.7	5.7	5.7	5.6	5.6	5.6
	08	44	91	88	56	63	94	41	98	64	11	57	02	74	45	17	87	58	28

Annex

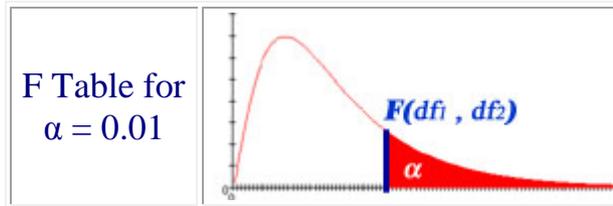
	6	3	4	2	1	1	2	0	8	4	7	8	5	4	9	0	7	1	1
5	6.6 07 9	5.7 86 1	5.4 09 5	5.1 92 2	5.0 50 3	4.9 50 3	4.8 75 9	4.8 18 3	4.7 72 5	4.7 35 1	4.6 77 7	4.6 18 8	4.5 58 1	4.5 27 2	4.4 95 7	4.4 63 8	4.4 31 4	4.3 98 5	4.3 65 0
6	5.9 87 4	5.1 43 3	4.7 57 1	4.5 33 7	4.3 87 4	4.2 83 9	4.2 06 7	4.1 46 8	4.0 99 0	4.0 60 0	3.9 99 9	3.9 38 1	3.8 74 2	3.8 41 5	3.8 08 2	3.7 74 3	3.7 39 8	3.7 04 7	3.6 68 9
7	5.5 91 4	4.7 37 4	4.3 46 8	4.1 20 3	3.9 71 5	3.8 66 0	3.7 87 0	3.7 25 7	3.6 76 7	3.6 36 5	3.5 74 7	3.5 10 7	3.4 44 5	3.4 10 5	3.3 75 8	3.3 40 4	3.3 04 3	3.2 67 4	3.2 29 8
8	5.3 17 7	4.4 59 0	4.0 66 2	3.8 37 9	3.6 87 5	3.5 80 6	3.5 00 5	3.4 38 1	3.3 88 1	3.3 47 2	3.2 83 9	3.2 18 4	3.1 50 3	3.1 15 2	3.0 79 4	3.0 42 8	3.0 05 3	2.9 66 9	2.9 27 6
9	5.1 17 4	4.2 56 5	3.8 62 5	3.6 33 1	3.4 81 7	3.3 73 8	3.2 92 7	3.2 29 6	3.1 78 9	3.1 37 3	3.0 72 9	3.0 06 1	2.9 36 5	2.9 00 5	2.8 63 7	2.8 25 9	2.7 87 2	2.7 47 5	2.7 06 7
10	4.9 64 6	4.1 02 8	3.7 08 3	3.4 78 0	3.3 25 8	3.2 17 2	3.1 35 5	3.0 71 7	3.0 20 4	2.9 78 2	2.9 13 0	2.8 45 0	2.7 74 0	2.7 37 2	2.6 99 6	2.6 60 9	2.6 21 1	2.5 80 1	2.5 37 9
11	4.8 44 3	3.9 82 3	3.5 87 4	3.3 56 7	3.2 03 9	3.0 94 6	3.0 12 3	2.9 48 0	2.8 96 2	2.8 53 6	2.7 87 6	2.7 18 6	2.6 46 4	2.6 09 0	2.5 70 5	2.5 30 9	2.4 90 1	2.4 48 0	2.4 04 5
12	4.7 47 2	3.8 85 3	3.4 90 3	3.2 59 2	3.1 05 9	2.9 96 1	2.9 13 4	2.8 48 6	2.7 96 4	2.7 53 4	2.6 86 6	2.6 16 9	2.5 43 6	2.5 05 5	2.4 66 3	2.4 25 9	2.3 84 2	2.3 41 0	2.2 96 2
13	4.6 67 2	3.8 05 6	3.4 10 5	3.1 79 1	3.0 25 4	2.9 15 3	2.8 32 1	2.7 66 9	2.7 14 4	2.6 71 0	2.6 03 7	2.5 33 1	2.4 58 9	2.4 20 2	2.3 80 3	2.3 39 2	2.2 96 6	2.2 52 4	2.2 06 4
14	4.6 00 1	3.7 38 9	3.3 43 9	3.1 12 2	2.9 58 2	2.8 47 7	2.7 64 2	2.6 98 7	2.6 45 8	2.6 02 2	2.5 34 2	2.4 63 0	2.3 87 9	2.3 48 7	2.3 08 2	2.2 66 4	2.2 22 9	2.1 77 8	2.1 30 7
15	4.5 43 1	3.6 82 3	3.2 87 4	3.0 55 6	2.9 01 3	2.7 90 5	2.7 06 6	2.6 40 8	2.5 87 6	2.5 43 7	2.4 75 3	2.4 03 4	2.3 27 5	2.2 87 8	2.2 46 8	2.2 04 3	2.1 60 1	2.1 14 1	2.0 65 8
16	4.4 94 0	3.6 33 7	3.2 38 9	3.0 06 9	2.8 52 4	2.7 41 3	2.6 57 2	2.5 91 1	2.5 37 7	2.4 93 5	2.4 24 7	2.3 52 2	2.2 75 6	2.2 35 4	2.1 93 8	2.1 50 7	2.1 05 8	2.0 58 9	2.0 09 6
17	4.4 51 3	3.5 91 5	3.1 96 8	2.9 64 7	2.8 10 0	2.6 98 7	2.6 14 3	2.5 48 0	2.4 94 3	2.4 49 9	2.3 80 7	2.3 07 7	2.2 30 4	2.1 89 8	2.1 47 7	2.1 04 0	2.0 58 4	2.0 10 7	1.9 60 4
18	4.4 13 9	3.5 54 6	3.1 59 9	2.9 27 7	2.7 72 9	2.6 61 3	2.5 76 7	2.5 10 2	2.4 56 3	2.4 11 7	2.3 42 1	2.2 68 6	2.1 90 6	2.1 49 7	2.1 07 1	2.0 62 9	2.0 16 6	1.9 68 1	1.9 16 8

Annex

19	4.3807	3.5219	3.1274	2.8951	2.7401	2.6283	2.5435	2.4768	2.4227	2.3779	2.3080	2.2341	2.1551	2.1141	2.0712	2.0264	1.9795	1.9302	1.8780
20	4.3512	3.4928	3.0984	2.8661	2.7109	2.5990	2.5140	2.4471	2.3928	2.3479	2.2776	2.2033	2.1242	2.0825	2.0391	1.9938	1.9464	1.8963	1.8443
21	4.3248	3.4668	3.0725	2.8401	2.6848	2.5727	2.4876	2.4205	2.3660	2.3210	2.2504	2.1757	2.0966	2.0549	2.0112	1.9655	1.9175	1.8677	1.8157
22	4.3009	3.4434	3.0491	2.8167	2.6613	2.5491	2.4638	2.3965	2.3419	2.2967	2.2258	2.1508	2.0715	2.0298	1.9860	1.9397	1.8914	1.8413	1.7891
23	4.2793	3.4222	3.0280	2.7955	2.6400	2.5277	2.4422	2.3748	2.3201	2.2746	2.2033	2.1280	2.0485	2.0068	1.9629	1.9165	1.8680	1.8177	1.7653
24	4.2597	3.4028	3.0088	2.7763	2.6207	2.5082	2.4225	2.3550	2.3002	2.2544	2.1828	2.1071	2.0273	1.9856	1.9415	1.8950	1.8463	1.7957	1.7430
25	4.2417	3.3852	2.9922	2.7597	2.6003	2.4876	2.4017	2.3341	2.2792	2.2332	2.1613	2.0853	2.0053	1.9636	1.9193	1.8725	1.8237	1.7734	1.7204
26	4.2252	3.3690	2.9772	2.7442	2.5846	2.4717	2.3855	2.3178	2.2627	2.2165	2.1443	2.0680	1.9878	1.9460	1.9021	1.8551	1.8060	1.7554	1.7023
27	4.2100	3.3541	2.9634	2.7298	2.5697	2.4566	2.3701	2.3022	2.2469	2.2005	2.1280	2.0515	1.9711	1.9292	1.8851	1.8378	1.7884	1.7375	1.6840
28	4.1960	3.3404	2.9507	2.7164	2.5555	2.4422	2.3553	2.2871	2.2316	2.1849	2.1120	2.0353	1.9546	1.9126	1.8683	1.8217	1.7730	1.7228	1.6700
29	4.1830	3.3277	2.9390	2.7041	2.5419	2.4284	2.3412	2.2727	2.2170	2.1700	2.0968	2.0200	1.9391	1.8970	1.8525	1.8057	1.7563	1.7050	1.6517
30	4.1709	3.3158	2.9283	2.6936	2.5289	2.4152	2.3277	2.2588	2.2028	2.1555	2.0820	2.0050	1.9238	1.8816	1.8370	1.7900	1.7413	1.6907	1.6380
40	4.0847	3.2317	2.8387	2.6060	2.4495	2.3359	2.2490	2.1802	2.1240	2.0772	2.0035	1.9265	1.8450	1.8027	1.7579	1.7105	1.6613	1.6101	1.5569
60	4.0012	3.1504	2.7581	2.5252	2.3733	2.2595	2.1722	2.1030	2.0464	1.9990	1.9248	1.8474	1.7655	1.7230	1.6779	1.6303	1.5811	1.5301	1.4771
1	3.939	3.030	2.626	2.424	2.222	2.121	2.020	1.919	1.919	1.818	1.717	1.616	1.515	1.414	1.414	1.313	1.212	1.111	1.010

Annex

20	71	80	47	89	75	86	16	58	10	33	50	58	08	54	95	29	51	53	
01	8	2	2	9	0	8	4	8	5	7	5	7	4	3	2	0	9	9	
∞	3.8	2.9	2.6	2.3	2.2	2.0	2.0	1.9	1.8	1.8	1.7	1.6	1.5	1.5	1.4	1.3	1.3	1.2	1.0
	41	95	04	71	14	98	09	38	79	30	52	66	70	17	59	94	18	21	00
	5	7	9	9	1	6	6	4	9	7	2	4	5	3	1	0	0	4	0



/	$df_1=1$	2	3	4	5	6	7	8	9	10	12	15	20	24	30	40	60	120	∞
d	40	49	54	56	57	58	59	59	60	60	61	61	62	62	62	62	63	63	63
f₂	52.	99.	03.	24.	63.	58.	28.	81.	22.	55.	06.	57.	08.	34.	60.	86.	13.	39.	65.
=	18	50	35	58	65	98	35	07	47	84	32	28	73	63	64	78	03	39	86
1	1	0	2	3	0	6	6	0	3	7	1	5	0	1	9	2	0	1	4
2	98.	99.	99.	99.	99.	99.	99.	99.	99.	99.	99.	99.	99.	99.	99.	99.	99.	99.	99.
	50	00	16	24	29	33	35	37	38	39	41	43	44	45	46	47	48	49	49
	3	0	6	9	9	3	6	4	8	9	6	3	9	8	6	4	2	1	9
3	34.	30.	29.	28.	28.	27.	27.	27.	27.	27.	27.	26.	26.	26.	26.	26.	26.	26.	26.
	11	81	45	71	23	91	67	48	34	22	05	87	69	59	50	41	31	22	12
	6	7	7	0	7	1	2	9	5	9	2	2	0	8	5	1	6	1	5
4	21.	18.	16.	15.	15.	15.	14.	14.	14.	14.	14.	14.	14.	13.	13.	13.	13.	13.	13.
	19	00	69	97	52	20	97	79	65	54	37	19	02	92	83	74	65	55	46
	8	0	4	7	2	7	6	9	9	6	4	8	0	9	8	5	2	8	3
5	16.	13.	12.	11.	10.	10.	10.	10.	10.	10.	9.8	9.7	9.5	9.4	9.3	9.2	9.2	9.1	9.0
	25	27	06	39	96	67	45	28	15	05	88	22	53	66	79	91	02	12	20
	8	4	0	2	7	2	6	9	8	1									
6	13.	10.	9.7	9.1	8.7	8.4	8.2	8.1	7.9	7.8	7.7	7.5	7.3	7.3	7.2	7.1	7.0	6.9	6.8
	74	92	80	48	46	66	60	02	76	74	18	59	96	13	29	43	57	69	80
	5	5																	
7	12.	9.5	8.4	7.8	7.4	7.1	6.9	6.8	6.7	6.6	6.4	6.3	6.1	6.0	5.9	5.9	5.8	5.7	5.6
	24	47	51	47	60	91	93	40	19	20	69	14	55	74	92	08	24	37	50
	6																		
8	11.	8.6	7.5	7.0	6.6	6.3	6.1	6.0	5.9	5.8	5.6	5.5	5.3	5.2	5.1	5.1	5.0	4.9	4.8
	25	49	91	06	32	71	78	29	11	14	67	15	59	79	98	16	32	46	59
	9																		
9	10.	8.0	6.9	6.4	6.0	5.8	5.6	5.4	5.3	5.2	5.1	4.9	4.8	4.7	4.6	4.5	4.4	4.3	4.3
	56	22	92	22	57	02	13	67	51	57	11	62	08	29	49	67	83	98	11
	1																		
10	10.	7.5	6.5	5.9	5.6	5.3	5.2	5.0	4.9	4.8	4.7	4.5	4.4	4.3	4.2	4.1	4.0	3.9	3.9
	04	59	52	94	36	86	00	57	42	49	06	58	05	27	47	65	82	96	09

Annex

	4																			
1	9.6	7.2	6.2	5.6	5.3	5.0	4.8	4.7	4.6	4.5	4.3	4.2	4.0	4.0	3.9	3.8	3.7	3.6	3.6	
1	46	06	17	68	16	69	86	44	32	39	97	51	99	21	41	60	76	90	02	
1	9.3	6.9	5.9	5.4	5.0	4.8	4.6	4.4	4.3	4.2	4.1	4.0	3.8	3.7	3.7	3.6	3.5	3.4	3.3	
2	30	27	53	12	64	21	40	99	88	96	55	10	58	80	01	19	35	49	61	
1	9.0	6.7	5.7	5.2	4.8	4.6	4.4	4.3	4.1	4.1	3.9	3.8	3.6	3.5	3.5	3.4	3.3	3.2	3.1	
3	74	01	39	05	62	20	41	02	91	00	60	15	65	87	07	25	41	55	65	
1	8.8	6.5	5.5	5.0	4.6	4.4	4.2	4.1	4.0	3.9	3.8	3.6	3.5	3.4	3.3	3.2	3.1	3.0	3.0	
4	62	15	64	35	95	56	78	40	30	39	00	56	05	27	48	66	81	94	04	
1	8.6	6.3	5.4	4.8	4.5	4.3	4.1	4.0	3.8	3.8	3.6	3.5	3.3	3.2	3.2	3.1	3.0	2.9	2.8	
5	83	59	17	93	56	18	42	04	95	05	66	22	72	94	14	32	47	59	68	
1	8.5	6.2	5.2	4.7	4.4	4.2	4.0	3.8	3.7	3.6	3.5	3.4	3.2	3.1	3.1	3.0	2.9	2.8	2.7	
6	31	26	92	73	37	02	26	90	80	91	53	09	59	81	01	18	33	45	53	
1	8.4	6.1	5.1	4.6	4.3	4.1	3.9	3.7	3.6	3.5	3.4	3.3	3.1	3.0	3.0	2.9	2.8	2.7	2.6	
7	00	12	85	69	36	02	27	91	82	93	55	12	62	84	03	20	35	46	53	
1	8.2	6.0	5.0	4.5	4.2	4.0	3.8	3.7	3.5	3.5	3.3	3.2	3.0	2.9	2.9	2.8	2.7	2.6	2.5	
8	85	13	92	79	48	15	41	05	97	08	71	27	77	99	19	35	49	60	66	
1	8.1	5.9	5.0	4.5	4.1	3.9	3.7	3.6	3.5	3.4	3.2	3.1	3.0	2.9	2.8	2.7	2.6	2.5	2.4	
9	85	26	10	00	71	39	65	31	23	34	97	53	03	25	44	61	74	84	89	
2	8.0	5.8	4.9	4.4	4.1	3.8	3.6	3.5	3.4	3.3	3.2	3.0	2.9	2.8	2.7	2.6	2.6	2.5	2.4	
0	96	49	38	31	03	71	99	64	57	68	31	88	38	59	78	95	08	17	21	
2	8.0	5.7	4.8	4.3	4.0	3.8	3.6	3.5	3.3	3.3	3.1	3.0	2.8	2.8	2.7	2.6	2.5	2.4	2.3	
1	17	80	74	69	42	12	40	06	98	10	73	30	80	01	20	36	48	57	60	
2	7.9	5.7	4.8	4.3	3.9	3.7	3.5	3.4	3.3	3.2	3.1	2.9	2.8	2.7	2.6	2.5	2.4	2.4	2.3	
2	45	19	17	13	88	58	87	53	46	58	21	78	27	49	67	83	95	03	05	
2	7.8	5.6	4.7	4.2	3.9	3.7	3.5	3.4	3.2	3.2	3.0	2.9	2.7	2.7	2.6	2.5	2.4	2.3	2.2	
3	81	64	65	64	39	10	39	06	99	11	74	31	81	02	20	35	47	54	56	
2	7.8	5.6	4.7	4.2	3.8	3.6	3.4	3.3	3.2	3.1	3.0	2.8	2.7	2.6	2.5	2.4	2.4	2.3	2.2	
4	23	14	18	18	95	67	96	63	56	68	32	89	38	59	77	92	03	10	11	
2	7.7	5.5	4.6	4.1	3.8	3.6	3.4	3.3	3.2	3.1	2.9	2.8	2.6	2.6	2.5	2.4	2.3	2.2	2.1	
5	70	68	75	77	55	27	57	24	17	29	93	50	99	20	38	53	64	70	69	
2	7.7	5.5	4.6	4.1	3.8	3.5	3.4	3.2	3.1	3.0	2.9	2.8	2.6	2.5	2.5	2.4	2.3	2.2	2.1	
6	21	26	37	40	18	91	21	88	82	94	58	15	64	85	03	17	27	33	31	
2	7.6	5.4	4.6	4.1	3.7	3.5	3.3	3.2	3.1	3.0	2.9	2.7	2.6	2.5	2.4	2.3	2.2	2.1	2.0	
7	77	88	01	06	85	58	88	56	49	62	26	83	32	52	70	84	94	98	97	
2	7.6	5.4	4.5	4.0	3.7	3.5	3.3	3.2	3.1	3.0	2.8	2.7	2.6	2.5	2.4	2.3	2.2	2.1	2.0	
8	36	53	68	74	54	28	58	26	20	32	96	53	02	22	40	54	63	67	64	

Annex

2	7.5	5.4	4.5	4.0	3.7	3.4	3.3	3.1	3.0	3.0	2.8	2.7	2.5	2.4	2.4	2.3	2.2	2.1	2.0
9	98	20	38	45	25	99	30	98	92	05	68	26	74	95	12	25	34	38	34
3	7.5	5.3	4.5	4.0	3.6	3.4	3.3	3.1	3.0	2.9	2.8	2.7	2.5	2.4	2.3	2.2	2.2	2.1	2.0
0	62	90	10	18	99	73	04	73	67	79	43	00	49	69	86	99	08	11	06
4	7.3	5.1	4.3	3.8	3.5	3.2	3.1	2.9	2.8	2.8	2.6	2.5	2.3	2.2	2.2	2.1	2.0	1.9	1.8
0	14	79	13	28	14	91	24	93	88	01	65	22	69	88	03	14	19	17	05
6	7.0	4.9	4.1	3.6	3.3	3.1	2.9	2.8	2.7	2.6	2.4	2.3	2.1	2.1	2.0	1.9	1.8	1.7	1.6
0	77	77	26	49	39	19	53	23	18	32	96	52	98	15	28	36	36	26	01
1	6.8	4.7	3.9	3.4	3.1	2.9	2.7	2.6	2.5	2.4	2.3	2.1	2.0	1.9	1.8	1.7	1.6	1.5	1.3
2	51	87	49	80	74	56	92	63	59	72	36	92	35	50	60	63	56	33	81
0	6.6	4.6	3.7	3.3	3.0	2.8	2.6	2.5	2.4	2.3	2.1	2.0	1.8	1.7	1.6	1.5	1.4	1.3	1.0
∞	35	05	82	19	17	02	39	11	07	21	85	39	78	91	96	92	73	25	00