ULTRASONOGRAPHY (OCULAR ECHOGRAPHY)

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INTRODUCTION

This chapter includes a review of:

- Introduction
- Theory
- Instrumentation
- Clinical indications and contra-indications
- Procedure
- Normal findings
- Abnormalities
- Orbital diagnosis

ULTRASONOGRAPHY

Ocular echography, or ultrasonography, is a commonly utilized technique to measure intraocular distances, including axial length, in clinical situations. In addition, ultrasound has become an important tool because it can be used to detect and characterize the soft tissue of the eye and orbit, even in the presence of intervening opacities. Diagnostically, it can also be used to detect, visualize and differentiate masses or foreign bodies within the structures of the eye.

Ultrasound is advantageous in comparison to other available imaging techniques in that it is non-invasive, produces no tissue irradiation or known side effects, is quick, convenient, and relatively inexpensive. It is also particularly well suited for soft tissue imaging. However, it has low resolution when compared to other techniques (e.g. magnetic resonance imaging or computed tomography) and is very dependent on examiner skill.

THEORY

Ocular echography involves the use of high frequency acoustic energy (sound waves) that is generally above the audible frequencies (usually above > 20 000 Hz). The typical frequencies used in diagnostic ophthalmic ultrasound are in the range of 1 to 25 MHz.The higher frequencies have shorter wavelengths and provide better spatial resolution than lower frequencies. However, the lower frequencies (and longer wavelengths) penetrate deeper into tissues before the energy is absorbed. The exact frequency used in ophthalmic work depends on the desired assessment. In general, high frequency ultrasound is used for measurements of the anterior segment while lower frequencies are used to determine axial length and to evaluate retrobulbar structures.

Acoustic (sound) waves penetrate through opaque tissues at varying speeds depending on the acoustic density of the tissue (Table 1). Acoustic impendence refers to the resistance of sound flow through a media and is dependent on acoustic density.

At the borders of density changes, the waves are reflected (echoes) or transmitted (refracted) according to the properties of the acoustic interface, namely its size, shape, smoothness and acoustic impedance. The acoustic impedance is a direct function of the density of the adjacent substances. The higher the acoustic density of a tissue, the greater is the impedance of the transmitted waves as well as the greater the reflection of echoes. Ultrasonography makes use of the resulting echoes and wave changes to determine the location and characteristics of the different tissues under examination.

Media	Sound Velocity (m/sec)
Water	1480
Aqueous (aqueous and vitreous)	1532
Cornea	1550
Soft Tissue	1550
Lens	1640
Bone	3500

Table 14.1: *Velocity at which sound waves penetrate through various tissues*

Adapted from: Eskridge JB, Amos JF and Bartlett JD. Clinical Procedures in Optometry. Lippincott, USA. 1991.

When ultrasound travel across different media, it can be reflected (echoes) and transmitted (refracted) in a manner similar to light, according to the properties of the interface (size, shape, smoothness) and the differences in acoustic impedances. For example, sound waves are directed at an interface between two tissues that have different acoustic impedances, the boundary between the two tissues acts as an acoustic mirror and an acoustic refracting surface. As a result, some of the ultrasound will be reflected (according to the Law of Reflection, i.e., the angle of reflection will be equal to the angle of incidence) and some will be transmitted. Ultrasonography makes use of the resulting echoes and wave changes to determine the location and characteristics of the different tissues under examination.

To measure the position of a given interface within the eye, ultrasound is transmitted to the eye from a transducer that contains a piezoelectric crystal. Piezoelectric crystals possess two important properties. First, the surfaces of these crystals are deformed (thus producing acoustic vibrations) when an electrical current is passed through the material. Second, when acoustic waves strike the crystal, they produce an electrical charge that can be recorded. Thus, if the transducer is positioned in such a manner that the acoustic waves intersect tissue interfaces in the eye in a perpendicular manner, sound is reflected and echo back to the transducer in proportion to the differences in the acoustic impedances of the different tissues.

Ultrasound instruments do not continuously emit sound waves. Instead, a procedure referred to as the "pulse-echo" technique is usually employed. With this technique a brief pulse of sound (typically 1 microsecond in duration) is emitted periodically. Between pulses, the instrument records the time that transpires between when the pulse was emitted and when the returning echoes produce a charge on the crystal. The elapsed times can be converted to distances between various interfaces and the probe simply by multiplying the measured time by the velocity of sound in the respective media.

Ultrasound does not travel at a constant velocity in the eye. It travels faster in the denser structures (e.g., the lens; 1640 m/sec) than it does in the less dense structures (e.g., the vitreous; 1530 m/sec). However, when an ultrasound instrument is used to measure axial length, it is generally assumed that sound travels at a constant velocity in the eye. In order to take into account the variations in intraocular acoustic velocity, a weighted "average" value for the velocity of sound within the eye is typically employed (e.g., 1540 m/sec). In aphakic patients (i.e., patients without a crystalline lens) it is necessary to assume a slightly lower velocity for sound than that employed with normal patients. Most commercially available ultrasound instruments now include, as an option, alternative operational settings for aphakic individuals.

For ophthalmic use, the time between echoes and the strength of the returning echoes are displayed in one of three ways: A-mode, B-mode or M-mode.

A-mode (A-scan, Amplitude mode) or biometry: the A-mode is the simplest and most commonly used ultrasound technique. With this technique the strength of the echo produced by a given interface is displayed as a vertical deflection (Y axis) relative to its position (time, X axis) along the path of the ultrasound beam.

The strength of the echo, which is related to the angle of the incident sound beam and the differences in acoustic impedance at the interface, is reflected in the height of the display deflection. A normal A-scan echograph obtained when the transducer is aligned with the optical axis is illustrated in Figure 14.1b.

Figure 14.1a: *Performing A-scan biometry*

Photo courtesy of: International Centre for Eye Health (ICEH), Photographer: B Ramamurthy.

The deflections associated with the anterior and posterior surfaces of the cornea and lens and the vitreoretinal interface allow measurements of corneal thickness, anterior chamber depth, lens thickness, vitreous chamber depth, and axial length. The aqueous and the vitreous should appear acoustically clear since they are normally homogenous structures.

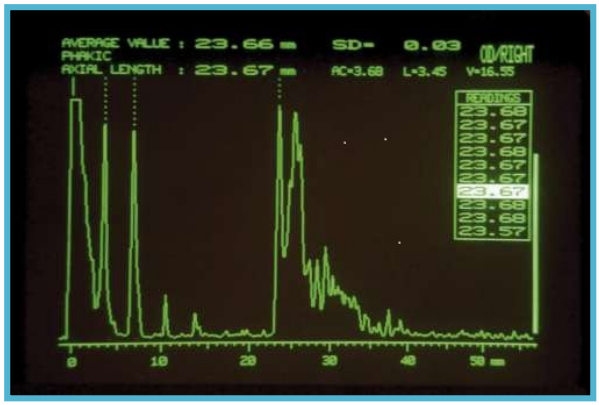


Figure 14.1b: *A-Mode Biometry*

Photo courtesy of: International Centre for Eye Health (ICEH), Photographer: B Ramamurthy.

B-mode (B-scan, Brightness mode). The B-mode is essentially composed of many bright echo spots resulting essentially from hundreds of A-scans. In the B-scan mode, the strength of the returning echo is indicated by an increase in the display brightness as a function of time or distance. Structures that produce tall echoes on A-scan (i.e. high reflecting tissues) will produce bright spots on B-scan.

In the B-mode, the spatial orientation of the transducer is systematically changed. The transducer orientation and the display orientation are coordinated so that a B-scan echograph looks like a cross section of the globe (two-dimensional image). The figure below shows a B-scan obtained along the vertical meridian of a normal eye. In the more sophisticated B-scan systems, the probe is oscillated in 2 dimensions allowing a 3 dimensional echograph of the eye to be constructed.

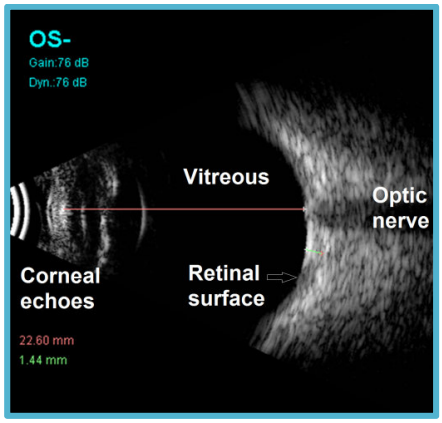


Figure 14.2: *B-Mode*

Photo courtesy of: LV Prasad Eye Institute.

Although the B-scan is a more involved procedure, it provides the most graphic representation of the relative positions of ocular structures and as a result, it is rapidly overtaking the A-scan as the most commonly utilized display technique. However, in comparison to the A-scan, the B-scan has historically been a much more complicated procedure. For example, instead of simply holding the transducer in contact with the eye or lids (as is typical with the A-scan) an immersion technique is sometimes required where the patient, usually in the supine position, is fitted with a set of adapted goggles that resemble a scuba diver mask with the plastic visor removed. The goggles are filled with a saline solution and the probe is placed in the solution. The liquid interface between the probe and the eye allows the probe to be moved (usually by a programmable mechanical device) without losing acoustic contact with the eye. More recently, B-scan probes have been manufactured so that the transducer is completely sealed within the probe (about 1.5 cm in diameter) and rotates about a point inside the probe so that a large scan of the posterior globe is possible simply by placing the probe in direct contact with the patient's lids.

M-mode (M-scan, Movement mode). In the M-mode the position and strength of the echoes are displayed as bright dots on the display. However, in contrast to the B-scan, the transducer is held stationary and the oscilloscope display (or film or light sensitive graph paper) is moved in "real time". With this display technique, movement of the tissues associated with accommodation, vascular pressure changes, etc., can be observed over time. It is often used in determining the magnetic properties of intraocular foreign bodies

INSTRUMENTATION

The ultrasound unit consists of a transmitter, a transducer, a receiver and a video unit. The transmitter produces the short electrical pulses that are sent to the transducer which contains a piezoelectric element, a polarized material (e.g. crystal) that can change shape and mechanically vibrate under an electrical stimulus thus generating ultrasound waves. Conversely, returning echoes deform the element which produces and electrical signal which is sent to the receiver.

The receiver is a radio-like device which essentially captures and amplifies the received sound frequencies.The video unit consists of an oscilloscope which allows the visualisation of the recorded signal.The B-scan unit has in addition a motor drive unit which moves (oscillates) the transducer along an axis (in order to generate multiple A-scans).

The ultrasonograms of interest are “frozen” or recorded when dynamic viewing is necessary and generally stored electronically.

Most ultrasound systems allow the examiner to perform A-mode and B-Mode simultaneously.A vector scan usually allows the selection of an axis of interest. The system contains a **vector scan** dial, which can be used to select any axis on the 2-dimensional image so as to assess specific areas and determine the spike amplitude or **reflectivity** of that tissue.

The amplitude or ‘gain’ of the ultrasound can be adjusted to increase or reduce the intensity of the returning echoes. Increasing the gain returns very low sound signals; this raises the sensitivity of the procedure but increases ‘noise’ levels or artefacts. Decreasing the gain will “remove” less acoustically dense tissue from the scan and enhance the visibility of the more acoustically dense tissues (which remain bright). The gain adjustment is different from the brightness or gray scale adjustment which modifies the overall contrast of the image.

CLINICAL INDICATIONS AND CONTRA-INDICATIONS

Ultrasound provides an accurate description of normal and abnormal structures even when the structure in question cannot be optically evaluated using visible light. While each procedure can be carried out alone, the A-mode and B-mode used in conjunction appear to provide the most complete ultrasonic evaluation. The A-mode provides the best means of evaluating the differences in acoustic impedances between tissues to provide accurate measurements of intraocular structures and lesions.

The B-mode provides a two-dimensional view of the eye and allows the topographic and kinetic assessment of ocular structures and lesions.Topographic echography reveals and documents the location, shape, borders and geographical relationships of lesions whereas various types of kinetic echography determine the vascularity, mobility and consistency of lesions.

Indications		Contra-indications
A-Mode	**B-Mode**	**A-Mode & B-Mode**
Assess axial length of the eye	Assess fundus through cloudy media	Recent intraocular surgery
Assess anterior chamber depth	Assess fundus through non-dilatable pupil	Perforating injury
Assess corneal thickness	Assess ocular & orbital lesions	Corneal disruption (+/-)
Intraocular lens power calculation	Assess optic nerve head disease (elevation)	
Differentiation of intra-ocular tumours	View surrounding orbital tissues (e.g. muscles)	
	Detect & differentiate ocular tumours	
	Locate intraocular foreign bodies	
	Characterize retinal detachments	
	Assess traumatized eyes	

Table 14.2: *Indications and contra-indications for A-mode and B-mode ultrasonography*

PROCEDURE

A-MODE

The patient is seated at an instrument similar to a slit lamp. A probe similar to a Goldmann tonometer is placed on the cornea or a hand held probe is applied directly to the cornea. Preliminary adjustments to the instrument include inputting patient data and keratometry readings, choosing biometry or pachymetry automatic mode and identifying phakia status.

Figure 14.3: *A-mode in a "Hand-held" set-up*

Photo courtesy of: International Centre for Eye Health (ICEH), Photographer: B Ramamurthy

The eye is first anaesthetized, and the probe sterilised in the usual manner. A drop of saline may be used on the probe tip, but the tear film is generally an acceptable coupling medium, which allows the transmission of acoustic waves from one surface to another. The patient is asked to fixate a distant target as the examiner brings the probe in contact with the central cornea. Care must be taken to avoid excessive force on the globe and to assure that the probe lies perpendicular to the plane of the central cornea. Once the probe is properly aligned, the sound waves traverse ocular contents and are reflected back at surface interfaces.

If the A-Mode is set at automatic, the system will sound when alignment is correct, indicating that a reading has been taken. The examiner should remove the probe and record the reading. Five readings should be taken on each eye. The system will average the readings of axial length, anterior chamber depth or corneal thickness. Keratometry readings and axial length measurement can be mathematically manipulated to calculate the power of the intra-ocular lens.

B-MODE

The patient is seated comfortably, or in a lying position. The probe may be applied either to the open or closed eye. Since high frequency sound waves are not transmitted through air, the probe must be coupled to the lid with a coupling agent, a thick and non-drip solution (usually methyl-cellulose). The patient should experience no discomfort during this procedure when performed through the closed lid. For the open eye procedure, anaesthetic is instilled prior and if necessary during the testing. The initial examination is performed at the highest decibel gain (sensitivity), so that even weak echoes from objects with low acoustic densities will be detected.

Performing B-Scan ultrasonography requires that the examiner perform axial, transverse and longitudinal scans of the globe to fully scan and map out the eye or lesions. The scanning probe has a marker near its tip, which designates the area represented on the upper portion of the B-Scan display. For the **axial views**, the patient fixates in primary gaze and the probe is placed with the marker superiorly for vertical sections and nasally for horizontally sections. In the **transverse views**, the probe is placed on the limbus and directed posteriorly. In a single smooth arc movement, it is moved from limbus to fornix, scanning the opposite globe wall from the posterior pole to the ora (postero-anteriorly). The scanning is repeated around the limbus (360°) to insure full coverage of the globe. The **longitudinal views** produce an antero-posterior slice of the opposite ocular wall along one meridian only, from ciliary body to optic nerve.The marker is oriented towards the cornea.

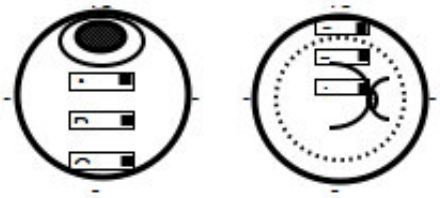


Figure 14.4: *Graphic representation of a transverse view showing probe position on the globe and the ocular area examined*

Figure 14.5: *Graphic representation of a longitudinal view showing probe position on the globe and the ocular area examined*

NORMAL FINDINGS

A-MODE

The characteristic display shows the left most echoes from the cornea and the next two echoes from the anterior and posterior lens surfaces. The echoes seen to the right are from the retina-choroid-sclera complex. The axial length and anterior chamber depth are noted in the upper right corner of the screen.

B-MODE

In the scan of the normal eye, the anterior portion of the eye is not clearly visualised (fig 14.2). The posterior lens capsule may be observed at the extreme left of the screen. The vitreous and optic nerve tissues reflect sound poorly and are termed **sonolucent** or **echolucent**. These structures appear black in contrast to structures that reflect sound well, which appear white or as shades of gray. The black horizontal V-shaped optic nerve is an important landmark in B-Mode ultrasonography. The retina appears as a smooth concave surface, which becomes indiscernible from the echoes arising from the choroid and sclera.

The **acoustic properties** of different tissue aid in diagnosis of abnormalities. Acoustically denser substances (e.g. calcium) will produce reflections even at low gain.

• Calcium • Retina, Choroid, Sclera • Haemorrhage • Vitreous tissue	↑ Increasing Acoustic Density (brighter echo)

ABNORMALITIES

VITREOUS ABNORMALITIES

The vitreous is normally sonolucent and will therefore appear dark and clear on ultrasonography especially in young patients. In older individuals, scattered opacities and posterior vitreous detachment will show up on A & B-scans with low reflectivity. Abnormal findings in the vitreous such as fibro-proliferative tissue, haemorrhages, membranes and inflammatory debris will appear as irregular white or gray areas. Acoustically denser findings such as asteroid hyalosis (calcium soaps) or foreign bodies will continue to appear on the scan as sensitivity is decreased.

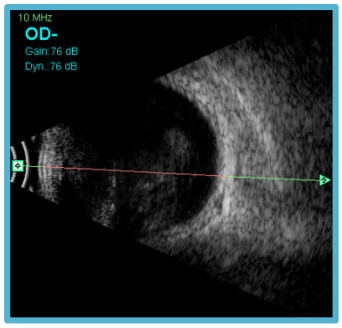


Figure 14.6a: *Vitreous haemorrhage*

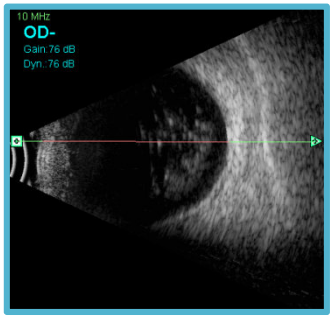


Figure 14.6b: *Asteroid Hyalosis*

Photos courtesy of: LV Prasad Eye Institute.

RETINAL ABNORMALITIES

Retinal detachment (RD) will appear as a thin white continuous folded membrane separate from the choroid and sclera (Fig.14.7). Many scans in serial planes are necessary to obtain the full three-dimensional extent of the RD. Flat RD is difficult to see because of the narrow space between the RD and the choroid. Bullous RD is convex in shape and extends into the anterior vitreous with attachments at the optic nerve head, nasal and temporal ora serrata. Fresh RD will move with eye movements, whereas long-standing RD will not because of associated fibrous tissue proliferation. The detached retina appears with very high reflectivity while the underlying space is generally sonolucent unless an haemorrhage exists underneath.

With classic retinoschisis, B-scan will differentiate an isolated “blister” from one with an underlying RD (Fig.14.8).

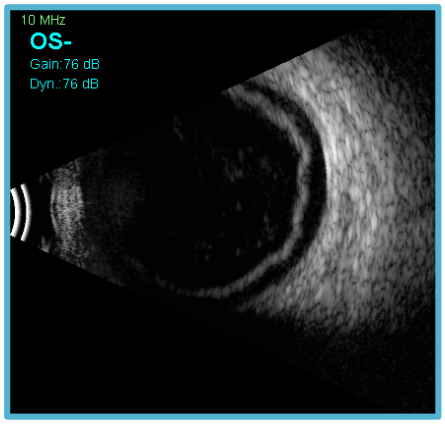


Figure 14.7: *Typical Retinal detachment*

Photo courtesy of: LV Prasad Eye Institute.

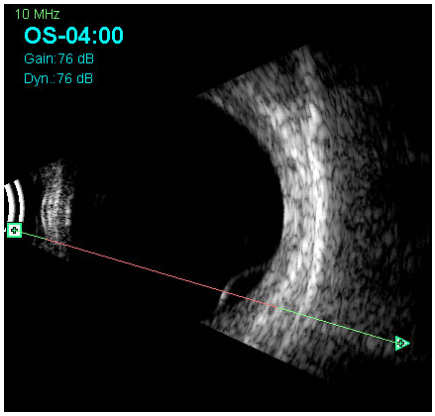


Figure 14.8: *Typical Retinoschisis*

Photo courtesy of: LV Prasad Eye Institute

INTRAOCULAR TUMOURS

Retinoblastoma in children is often concealed ophthalmoscopically by an overlying retinal detachment, inflammation or vitreous haemorrhage. The retinoblastoma which is acoustically dense will have high reflectivity and can be differentiated using B-scan. Osseous choristoma, a rare bone tumour of the choroid, is also acoustically diagnostic by its high reflectivity.

Choroidal tumours can be differentiated from choroidal detachments with underlying serous fluid or blood. Certain characteristics differentiate malignant melanomas from metastatic carcinoma, haemangioma, & subretinal haemorrhage.

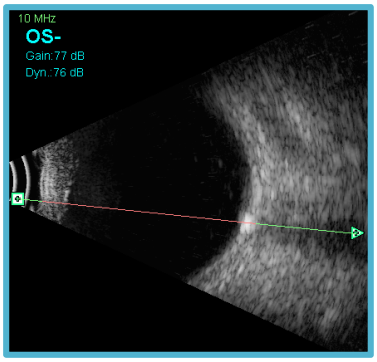
Lesion	Internal Structure (Cells)	Internal Reflectivity	Sound Attenuation
Melanoma	Small & Regular	Low to Medium	Significant
Metastasis	Irregular	Variable	Variable
Haemangioma	Large & Regular	High	Minimal

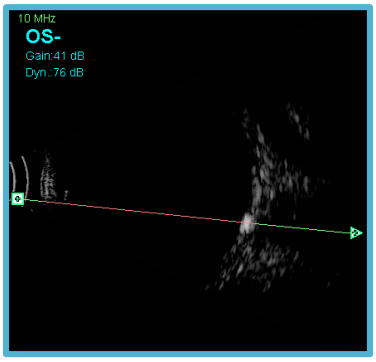
Table 14.3: *Response of various lesions when performing ultrasonography*

OPTIC NERVE HEAD ABNORMALITIES

Conditions that result in elevation of the optic nerve head, such as papilloedema, papillitis and drusen of the optic disc can be appreciated ultrasonically. Drusen bodies often give the appearance of grape clusters (Fig. 14.9 a and b). However, buried drusen are not visible to the eye and is the most common cause of pseudo-papilloedema. Ultrasonography will show the high reflectivity of the calcium within the drusen and the continued reflection of sound as sensitivity is decreased.

Papillitis and papilloedema are difficult to differentiate ultrasonically although a clear subretinal fluid level may be seen with papilloedema. Peripapillary staphyloma will be seen as a concave depression at the position of the optic nerve head.

A 



B

Figure 14.9a. and b.: *Optic nerve head drusen*

INTRAOCULAR FOREIGN BODY

Ultrasonography is used to locate foreign bodies and to assess their magnetic properties. Localisation requires decreasing the decibel gain to differentiate the high amplitude echoes produced by most foreign bodies from lower amplitude echoes emanating from surrounding tissue. Magnetic foreign bodies can be identified by using an ultrasonic display of the motion of the foreign body when a magnet is applied to the globe, placed in a position over the pars plana. The finding of metallic intraocular foreign bodies is an obvious contraindication to performing magnetic resonance imaging.

LENS DISLOCATION OR SUBLUXATION

Subluxated or dislocated lenses secondary to trauma or associated systemic disorders are difficult to view ophthalmoscopically. Ultrasonography is a useful tool in these cases.

GLOBE SHAPE AND SIZE VARIATION

Eyes with opaque media and especially low intraocular pressures are suggestive of phthisis bulbi. Ultrasonography will show disorganized tissue of high reflectivity.

ORBITAL DIAGNOSIS

Ultrasonography of the orbit is useful when there is proptosis or exophthalmos, choroidal folds or retinal striae, unexplained optic atrophy or papilloedema, palpation of a cyst or mass, microphthalmic eye, and suspected orbital foreign body. In the orbit, the abnormal appears dark against the white bright background of highly acoustic dense orbital fat (versus in the globe where the abnormal is white or gray on a black background).Abnormalities that appear black include mass lesion, foreign body and inflammatory change.

Extra-ocular muscles in the orbit are sonolucent and normally appear black.Enlargement and infiltration of the muscles will render them abnormally white on ultrasonography.

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FLUORESCEIN ANGIOGRAPHY

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INTRODUCTION

This chapter includes a review of:

- Definition
- Purpose
- Indications
- Contra-indications (relative)
- Technique principle
- Procedure
- Factors affecting visualization
- Interpretation
- Terminology
- Interpretation steps of Fluorescein Angiography
- Indocyanine green angiography

DEFINITION

Fluorescein Angiography (FA) is a technique used to dynamically evaluate vascular conditions of the eye by photographing Sodium Fluorescein (NaFl) dye in the vasculature following intravenous (IV) injection. FA allows the visualisation of the normal passage of blood (dye) from the arterial to the venous systems in both the retinal and choroidal circulations of the eye. Pathological changes on blood vessels which affect the vascular circulation and the inner or outer blood-retinal barrier can also be viewed with FA.

PURPOSE

- Advanced understanding of ocular vasculopathies reveals that earlier disease diagnosis and treatment yields better clinical results.
- Progress in laser therapeutics permits very early intervention in disease conditions.
- FA permits earlier and more effective detection of disease processes that may be otherwise subclinical and not observable ophthalmoscopically. FA enables viewing retinal details as small as 5 microns compared to direct ophthalmoscopy which permits viewing of details > 72 microns even with 15X magnification.

INDICATIONS

1. Suspected or possible Sub-Retinal Neovascular Membranes (SRNVM)
2. Proliferative vascular changes (e.g. diabetes mellitus)
3. Suspected “leaking” problems of the retina or choroid (e.g. macular oedema))
4. Unexplained visual loss
5. Unidentified Fundus Observation (Tumours, Drusen, etc.)
6. Suspected diseases of the RPE/Bruch Membrane complex (e.g. dystrophies).

OCULAR DISEASE CONDITIONS INDICATING THE NEED FOR FA

- Acute posterior multifocal placoid pigment epitheliopathy (APMPPE)
- Angiomatosis retinae
- Anterior ischemic optic neuropathy
- Behcet’s disease
- Branch retinal vein occlusion
- Cavernous haemangioma of the retina
- Choroidal rupture (when developing choroidal neovascularisation)
- Coat’s disease
- Cystoid maculopathy (Irvine-Gass syndrome)
- Diabetic retinopathy
- Eales disease
- Fuch’s spot
- Hemicentral retinal vein occlusion
- Idiopathic central serous choroidopathy
- Iris neovascularisation
- Maculopathy of angioid streaks
- Malignant choroidal melanoma
- Preretinal macular fibrosis
- Presumed ocular histoplasmosis (macular changes)
- Proliferative peripheral retinal disease
- Retinal capillary haemangioma
- Retinal microaneurism
- Retinal pigment epithelial dystrophies (central)
- Retinal pigment epithelial detachment
- Retinal tumours
- Sensory retinal detachments
- Tumours of iris and ciliary body.

CONTRA-INDICATIONS

- Frail Health
- Cardiac/Bronchial Disease
- Renal Diseases
- Hypersensitive Status
- Asthma (poorly controlled)
- Severe diabetes mellitus
- Hypertension
- Hypersensitivity to NaFl
- Pregnancy / Lactating mother.

TECHNIQUE PRINCIPLE

Sodium Fluorescein (NaFl) is a pharmacologically inactive substance which fluoresces when stimulated by an exciting light source. The substance may be available in solution concentrations of 5%, 10% and 25%. Absorbing light maximally at 485nm (blue), it emits maximally (peak transmission) at 520nm (green). In the bloodstream, when IV injected or orally ingested, it can be visualised at the ocular level by several methods:

- **Direct** with a BIO equipped with special filters
- **Video-based** system equipped with special filters permitting live recording of the Fluorescein flow
- **Photography** on standard 35mm negatives or positives viewed on a lighted box.

Photography is the usual method of performing FA. The procedure requires a special fundus camera which includes a high intensity flash with rapid recycle time delay (1 - 1,5 sec) to allow “rapid fire” serial photographs and a timer to register interval from injection time to picture time. A 36 exposure black and white film (200-400 ASA or Kodak Tri-X film) is usually used.

The camera is adapted to contain two special filters. The excitation filter is a blue filter of wavelength 465-490 nm [Baird Atomic B4 470 or Kodak Wratten 47]. Placed between the illumination system of the camera and the retina, it serves to excite and raise the NaFl electrons to a higher energy level causing them to fluoresce. The barrier filter is a yellow-green filter of wavelength 525-630nm [Iford 109 Delta Chromatic 3 or Kodak Wratten g15]. Placed between the light reflected from the retina and the camera film plane, it blocks the emitted light except the light from the excited NaFl (λ ~ 525nm) to allow the viewing and imaging of fluorescing tissues and blood.

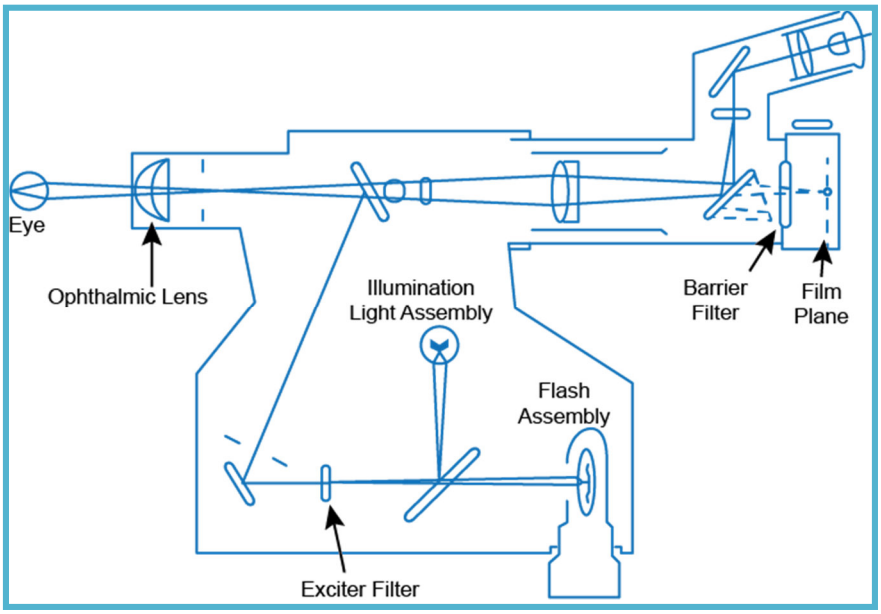

Figure 15.1: *Optics of the camera used in FA*

PROCEDURE

INTRA-VENOUS

- Have a crash cart (cardiopulmonary resuscitation unit) and emergency protocol on site
- Educate patient and obtain consent signature
- Maximum pupillary dilation required
- Seat patient comfortably and appropriately at fundus camera
- Direct patient fixation, which must be maintained throughout the procedure
- Obtain colour fundus photos (stereo pairs preferable)
- Obtain baseline red-free (green or Wratten 57) photos on black/white film through system filters
- Check for pseudofluorescence as a result of poor filter quality
- Ensure that proper filters and flashes are in place
- Set appropriate IV line on antecubital vein or hand vein and maintain with heparinised saline.
- Set 5ml NaFl 10% (preferred dosage) ready in a syringe for injection (or 10ml of 5% or 3ml of 25%)
- Locate and focus area of interest in the fundus
- Inject bolus of NaFl regularly over 10-15sec.
- Start photo shoot 10-15 sec later (time for NaFl to reach ocular circulation)
- Shoot rapid sequence photos first minute: 1 per 1-2 sec. first 15 sec.\ 1 per 10-15 sec. next 45 sec.
- Next 10-20 minutes shoot intermittently at regular time intervals (e.g. 1 per minute)
- Shoot photos of fellow eye after primary eye is done
- Shoot stereo pairs when possible

SIDE-EFFECTS

The procedure is relatively safe with a clinical dose of 100 X less than the lethal dose of NaFl but complications arise in ~ 5% of IV procedures (Table 1). Occurring during the first 30 sec. of the procedure, these are usually minor and transient. However cardiac arrest and even death can occur.

Common (in 5% of procedures within 30 sec)	Less Common
Nausea	Cardiac arrest
Warm flush	Respiratory reactions
Vomiting	Acute pulmonary oedema
Urticaria and pruritus (hives and itching)	Seizures
Skin discolouration (yellowing for ~1 hour)	Extravasation
Urine discolouration (yellow-orange for ~24 hours)	
Syncope	

Table 15.1: *Complications of IV procedures*

ORAL FLUOROGRAPHY

Oral Fluorography provides similar results but is not as good or as clear as IV FA. As such, it is not so valuable for the observation of fine details but it is especially useful when expected late dye leakage is of interest. With minimal to no side-effects, it is much safer than IVFA and may be used for children and patients with cardiovascular compromise. The procedure includes similar observation elements but with the following technical changes:

- Patient must fast 8 hours before exam
- NaFl is given orally: 15ml of 10% NaFl with citrus solution over crushed ice
- Dentures must be removed to avoid staining
- Red-free photos are taken before ingestion
- Photo shoot starts 15-30 min. after ingestion - must look for 1st sign of fluorescence in the fundus
- Late phases are ~ 1 hour after ingestion.

FACTORS AFFECTING VISUALISATION

- Clarity of media
- Dilation level
- Quality of camera
- Skill of examiner
- Patient cooperation
- NaFl concentration reaching the eye (depends most on injection quality)
- Quality of film processing
- Quality of filters (need regular changes) which can cause pseudofluorescence.

INTERPRETATION

The interpretation of FA is based on basic anatomical and physiological principles. Good knowledge of these is crucial to the understanding of FA.

Inner blood-retinal barrier - Healthy retinal vessels are impermeable to NaFl and are not leaky.

Fenestrated choriocapillaris - Healthy choriocapillaris is a sponge-like tissue whose vessels are fenestrated (porous). Hence blood and NaFl freely leak from it.

Outer blood-retinal barrier - Healthy RPE-Bruch complex with the tight “zonula occluden” junctions between RPE cells keeps blood (and NaFl) of the choroid and choriocapillaris away from the retina.

RPE filter - the RPE acts like an optical filter. The “choroidal glow” that results from the NaFl freely leaking within it only shows through partially, giving a typical **ground-glass appearance**.

Macular hypofluorescence - Dense cuboidal RPE and xantophyll mask the “choroidal glow” across healthy maculae.

TERMINOLOGY

Hyperfluorescence indicates more glow (NaFl) than would be normally expected (e.g. leakage, pooling, RPE faults...)

Hypofluorescence indicates less glow (NaFl) than would by normally expected (e.g. non-perfusion, blockage,...)

Autofluorescence refers to the ability of certain retinal components to fluoresce naturally without the presence of NaFl. The pre-injection as well as the black and white control photo through the camera filters allows the differentiation of autofluorescent elements (e.g. ONH drusen, myelinated NF,...)

Pseudofluorescence results from the overlap of the transmission curves of exciter and barrier filters that may result in apparent fluorescence. The pre-injection as well as the black and white control photo through camera filters also allows the detection of pseudofluorescence.

Transit refers to the time of the first passage of fluorescing blood in the eye (arm-retina cycle). Although it varies with the dynamics of blood circulation factors such as cardiac output, blood volume, etc., it is usually from 10-20 sec.

Recirculation Phase refers to subsequent passages of fluorescing blood in the eye. Recirculation phases are less intense.

Phases refer to specific physiological intervals in the FA cycle. Phases occur quite rapidly and may overlap with one another.

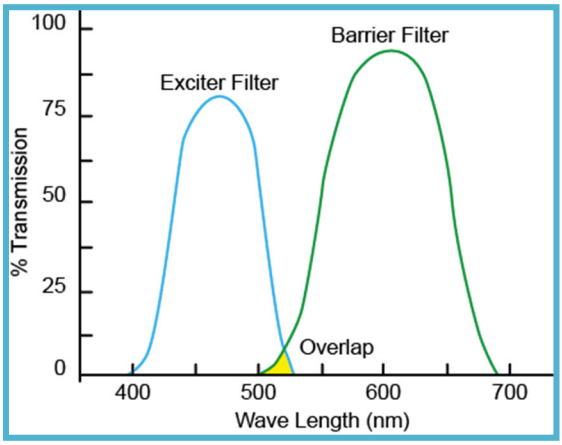

Figure 15.2: *Phases of the FA cycle*

Adapted from Eskridge JB, et al, Clinical Procedures in Optometry, Philadelphia, PA: J.B.Lippincott Company, 1991.

1. Choroidal Flush (7-10 sec. after injection)

The choroidal flush corresponds to the rapid "patchy" filling of the choroidal system (long and short ciliary arteries) with fluorescing blood (Fig. 15.3). Because of the fenestrated vessels of the choroid, the NaFl quickly leaks in the choroidal swamp and the choroidal glow becomes somewhat uniform. The RPE partly masks the choroidal flush to give it a "ground-glass" appearance; this stage occurs first as the choroidal circulatory route is slightly shorter than the retinal route. The Cilio-retinal artery fills at this stage because it originates from the choroidal vasculature.

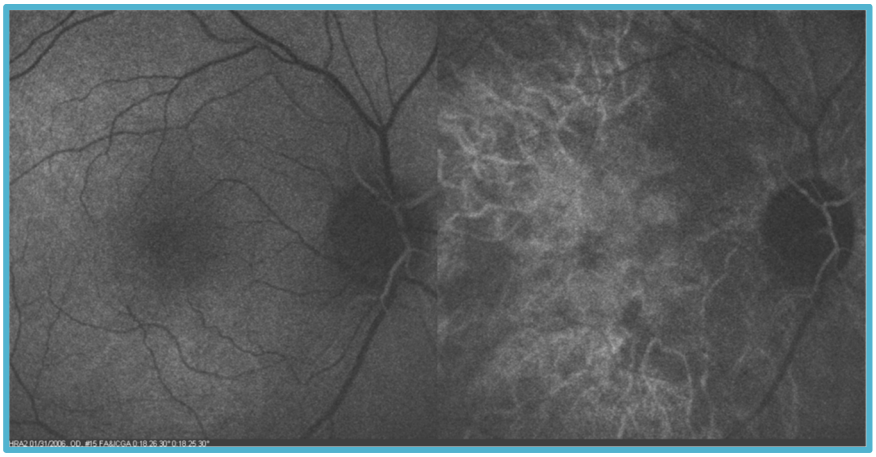

Figure 15.3: *Choroidal phase of FA cycle*

Photo Courtesy of Priyashangu Chandra: LV Prasad Eye Institute.

2. Arterial Phase (11-12sec. after injection)

The arterial phase corresponds to the filling of the Central Retinal Artery and retinal arteries. **Laminar flow** becomes observable (Fig. 15.4 and 15.5): blood flow dynamics make the arterial core glow before the arterial walls. This is followed by complete filling of the arteries (Fig. 15.6).

Figure 15.4: *Black indicates non-fluorescence; white area indicates fluorescence*

Figure 15.5: *Early arterial phase of FA cycle showing laminar flow*

Photo Courtesy of LV Prasad Eye Institute.

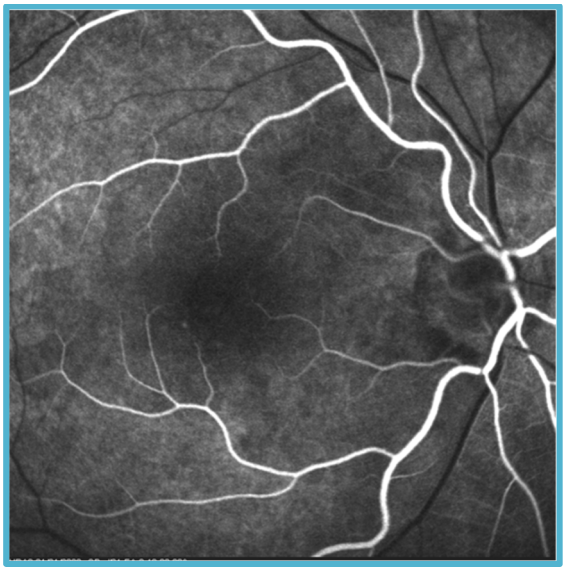

Figure 15.6: *Arterial phase of FA cycle*

Photo Courtesy of LV Prasad Eye Institute.

3. Arterio-Venous (A-V) Phase (13-15sec. after injection)

The A-V phase corresponds to the filling of capillaries in the interval between arterial and venous circulation (Fig. 15.7).

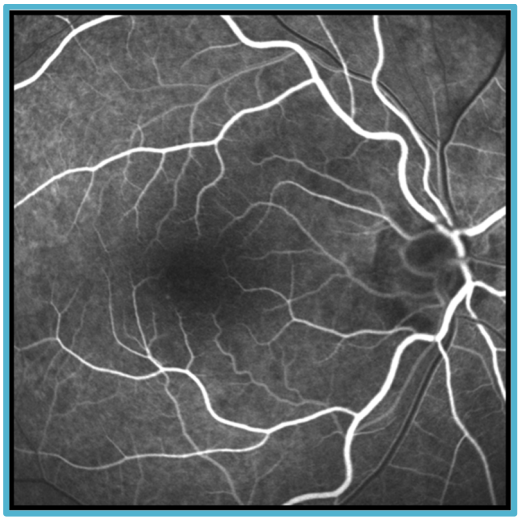

Figure 15.7: *Arteriovenous phase of FA cycle*

Photo Courtesy of LV Prasad Eye Institute

4. Venous Phase (16-20sec. after injection)

The venous phase corresponds to the filling of retinal veins. The laminar flow is initially observable but this time the venous wall glows before the venous core (Fig. 15.8 and 15.9). Laminar flow ceases at ~ 18-20sec. in the late venous phase when the veins are fully filled (Fig. 15.10).

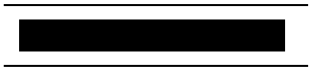

Figure 8. Black indicates non-fluorescence; white area indicates fluorescence

Figure 15.9: Early venous phase of FA cycle showing laminar flow

Photo Courtesy of LV Prasad Eye Institute.

Figure 15.10: *Late venous phase of FA cycle*

Photo Courtesy of LV Prasad Eye Institute.

5. Late Phase (~ 10minutes post-injection)

The late phase is the recirculation stages when the arteries and veins are empty of NaFl. The choroidal flush is minimised and the ONH hyperfluoresces because NaFl adheres to the scleral rim and nervous tissue (this glow is constant throughout the procedure and does not diffuse if the tissue is normal) (Fig. 15.11).

Figure 15.11: *Phases of the FA cycle*

Photo Courtesy of LV Prasad Eye Institute.

Leakage and **Pooling** become more apparent as NaFl diffuses into surrounding tissues. Leakage occurs with the extravasation or escape of fluorescing blood and indicates retinal vascular abnormality. Pooling represents accumulation of fluid and generally indicates a break in the RPE-Bruch barrier.

Note: Some authors prefer to use “Arterio-Venous Phase” to speak of stages 2,3,4 jointly.

INTERPRETATION STEPS OF FLUORESCEIN ANGIOGRAPHY

1. Study the colour photographs
2. Study the red-free photos (see everything)
3. Note the time, phase, location at all times
4. Look for hyper and hypofluorescence
5. Study frame by frame changes in size and intensity.

E.g. At 17 seconds, late choroidal filling phase, the OD shows 1 spot of hyperfluorescence in the inferior paramacular area. It is observed to percolate upward increasing in size and intensity throughout the test.

INTERPRETATION OF FLUORESCEIN ANGIOGRAPHY

Broadly two things need to be considered:

1. Hypofluoresce versus hyperfluoresce
2. Timing or delay in fluorescence.

Hypofluorescence	Hyperfluorescence →	Angiographic Features
Vascular filling defect	**Transmission defects** ⇐ atrophy of RPE revealing choroidal fluorescence	
Vascular occlusion Emboli Arteriosclerosis Vascular nonperfusion	Window defects Age-related macular degeneration pigment changes Retino-choroidal dystrophies Choroidal Rupture	⇐ Hyperfluorescence increases and decreases in phase with the FA
Blocked fluorescence	**Things that leak** ⇐ breakdown of inner retinal barrier	
Haemorrhages Exudates Cotton wool spots Glial tissue Retinal Pigment Masses	Microaneurisms Neovascularization Intra-retinal microvascular abnormalities Disruption of vessel integrity e.g. wet ARMD	⇐ Early intense leakage increasing throughout the FA
	Things that pool ⇐ breakdown of outer retinal barrier	
	Cystoid Macular Oedema Idiopathic Central Serous Choroidopathy Serous detachment of the RPE Papilloedema	⇐ Slowly increasing hyperfluorescence throughout the FA and after
	Things that stain ⇐ uptake of NaFl into tissues	
	Optic nerve head drusen Retinal Drusen Optic nerve head scleral rim and tissues Sclera Vessel Walls	⇐ Slow staining that does not diffuse or increase in size throughout the FA

Table 15.2: *Interpretation of FA*

INDOCYANINE GREEN ANGIOGRAPHY (ICG)

Indocyanine Green (ICG) is a relatively new procedure. ICG is advantageous over FA in that the ICG dye fluoresces near the infrared spectrum with peak absorption at 805nm and peak fluorescence at 835nm. This enhances the fluorescence through exudates, haemorrhages and normal ocular pigment (RPE). Being 98% protein-bound in the blood, the dye does not readily leak through the fenestrations of the choriocapillaris or neo-vessels. Therefore it does not obscure the underlying choroidal vasculature.

An improved visualization of the choroid is obtained with ICG because it permits a longer and uninterrupted view of the choroidal circulation. As such, it is primarily used to expose or define sub-retinal neo-vascular membranes (SRNVM) when they are suspected but not seen with NaFl angiography. ICG can however be used for all the same clinical applications as NaFl.

The only contra-indication to ICG is an allergy to shell fish or to iodine.