# ENZYMATIC ASSISTED VITRECTOMY

**Essay**

*Submitted for partial fulfillment of master degree inOphthalmology*


**Submitted by**

**Mahmoud Abdalla Mostafa Hasan**

*M.B.B.Ch.*

**Under Supervision of**

*Prof. Dr. Tarek Ahmad Al-Mamoun*

*Professor of Ophthalmology - Ain Shams University*

*Prof. Dr. Mohammad Ahmad Rashad*

*Professor of Ophthalmology - Ain Shams University*



Faculty of Medicine

Ain Shams University

2014

بسم الله الرحمن الرحيم

# قالوا سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم

صدق الله العظيم
سورة البقرة – الآية 32

# Table of contents

# List of figures

# List of Tables

# List of Abbreviations

| | |
|---|---|
| **APE** | Autologous plasmin enzyme |
| **$Arg^{561}$** | Arginine amino acid |
| **ARMD** | Age related macular degenerations |
| **$Asp^{646}$** | Asparagine amino acid |
| **AU** | Activity unit |
| **BCVA** | Best corrected visual acuity |
| **BRB** | Blood retinal barrier |
| **BSS** | Buffered saline solution |
| **CME** | Cystoid macular edema |
| **CMT** | Central macular thickness |
| **CS** | Chondroitin sulfate |
| **DME** | Diabetic macular edema |
| **ECM** | Extracellular matrix |
| **EM** | Electron microscopy |
| **ERG** | Electroretinogram |
| **ERM** | Epiretinal membrane |
| **FDA** | Food and drug administration |
| **FMERG** | Focal macular Electroretinogram |
| **FU** | Fibrin degradation unit |
| **GAGs** | Glycosaminoglycans |
| **HA** | Hyaluronic acid |
| **$His^{603}$** | Histidine amino acid |
| **ILL** | Internal limiting lamina |
| **ILM** | Internal limiting membrane |
| **IOP** | Intra-ocular pressure |
| **IU** | International units |
| **KDa** | Kilo Daltons |
| **LM** | Light microscopy |
| **MC** | Muller cell |
| **MCFP** | Muller cell foot plate |
| **MEM** | Macular epiretinal membrane |
| **MMP-3** | Matrix Metalloproteinase-3 |
| **MMPs** | Matrix Metalloproteinases |

| | |
|---|---|
| **MW** | Molecular weight |
| **OCT** | Optical coherence tomography |
| **PAS** | Periodic acid Schiff |
| **PBS** | Phosphate buffered saline |
| **PDR** | Proliferative diabetic retinopathy |
| **PNLs** | Polymorphneuclear leukocytes |
| **PVD** | Posterior vitreous detachment |
| **PVR** | Proliferative vitreoretinopathy |
| **RD** | Retinal detachment |
| **r-Lys-Plg** | Recombinant lysine plasminogen |
| **r-mPlg** | Recombinant microplasminogen |
| **ROP** | Retinopathy of prematurity |
| **RPE** | Retinal pigment epithelium |
| **RRD** | Rhegmatogenous retinal detachment |
| **r-SK** | Recombinant streptokinase |
| **r-UK** | Recombinant urokinase |
| **RVO** | Retinal vein occlusion |
| **SDOCT** | Spectral domain optical coherence tomography |
| **SEM** | Scanning electron microscopy |
| **$Ser^{741}$** | Serine amino acid |
| **SF6** | Sulphar hexafluoride |
| **TA** | Triamcinolone acetonide |
| **TEM** | Transmission electron microscopy |
| **TG-MV-006** | Code name of the study |
| **TG-MV-007** | Code name of the study |
| **tPA** | Tissue plasminogen activator |
| **UK** | Urokinase |
| **UKr** | Urokinase receptor |
| **VA** | Visual acuity |
| **$Val^{562}$** | Valine amino acid |
| **VMA** | Vitreomacular adhesion |
| **VMT** | Vitreomacular traction syndrome |

# Introduction

For a long time the vitreous has been overlooked as a crucial element in the patho-physiology of various blinding disorders. This has begun to change in the light of advances in knowledge of the structure, function and the pathobiology of that unique matrix. The posterior vitreous cortex adheres to the inner retinal surface in the normal human eye at the vitreous base, the optic disc, along the major retinal vessels and to the entire posterior pole ***(Sebag, 1991).***

Spontaneous posterior vitreous detachment (PVD) and vitreous liquefaction can develop as an age related change in the human eye. Separation of the vitreous from the fovea can alleviate macular traction, this greatly reduces the risk of macular hole formation***(Akiba et al., 1990).***

Complete PVD may also prevent retinal neo-vascularization in eyes with diabetic retinopathy and retinal vein occlusion. The separation of the vitreous from the retina is an important and critical step invitreous surgery, because the mechanical creation of PVD often leads to complications ***(Akiba et al., 1990).***

Vitreo-retinal surgical proceduresare developed to relieve vitreous tractions and adhesions to facilitate reattachment of a detached retina or to reduce retinal edema. This is greatly dependent on the presence or absence of PVD and the degree of adhesions between the vitreous and the retina ***(Sebag, 1987).***

Diseases such as proliferative vitreoretinopathy (PVR), macular hole and proliferative diabetic retinopathy (PDR) are associated with pathologic changes at the vitreo-retinal interface induced by anomalous PVD ***(Sebag, 2004).***

The surgical techniques and the instruments of vitreous surgery have been improved greatly but the surgery still risky and difficult in some cases. Iatrogenic retinal breaks, retinal detachment (RD) and retinal nerve fiber damage may develop specially in younger patients ***(Han et al., 1998).***

The pharmacological vitrectomy that is used to induce PVD and to liquefy the vitreous gel without damaging the retina is the main substitute of mechanical vitrectomy. Such vitrectomy uses a group of enzymatic agents to digest specific components of extracellular matrix at the vitreo-retinal interface to form PVD and in the gel to be liquefied. Enzymatic vitrectomy has many advantages such as fewer surgical complications, less surgical time and lower operation costs ***(Trese et al., 2000).***

Many methods have been developed to produce liquefaction of the vitreous body and to relieve adhesions at the vitreoretinal interface. This will lead to separation and collapse of corpus vitreum to facilitate surgery or even to replace it ***(Czajka and Pecold, 2002).***

The enzymes used in enzymatic vitrectomy can be classified into two groups; Vitreous liquefaction enzymes such as Hyaluronidase, Collagenase and Streptokinase and PVD inducing enzymes such as Plasmin, Dispase and Chondroitinase ***(Trese et al., 2000).***

Plasmin and its recombinant ocriplasmin (formerly known as microplasmin)have received the most attention and appear to be the most useful enzymes. They are non-specific proteases that can be isolated from patient's own serum ***(Sakuma et al., 2003).***

Plasmin mediated fibrinolysis has properties to hydrolyze a variety of glycoprotein components of the vitreo-retinal interface. These glycoprotein components are laminin and fibronectin. Their hydrolysis will lead to degradation of the links between the vitreo-retinal interface and the internal limiting membrane. This in turn is sufficient to induce posterior vitreous detachment ***(Gandorfer et al., 2004).***

# Aim of the work

This essay aims to review the literature in the role of enzymes in vitrectomy.

# Vitreous Anatomy

## Macroscopic structure of the vitreous

In the emmetropic adult human eye, the corpus vitreum is approximately 16.5 mm in axial length with a depression anteriorly just behind the lens called the patellar fossa. The hyaloideocapsular ligament of Wieger is the annular region 1-2 mm in width and 8-9 mm in diameter where the corpus vitreum is attached to the posterior aspect of the lens.Itis stronger in youth than in old age and is sufficiently weak to permit intra capsular lens extraction without pulling on the anterior vitreous face. Berger's space is at the center of the hyaloideocapsular ligament (Fig. 1)***(Anthony et al., 1997).***

The corpus vitreum is a transparent colorless gel like substance of consistency firmer than egg white.Vitreous volume is about 3.9ml which fills the posterior four fifths of the globe and weighs approximately 4gm. It is in contact with the retina behind and the ciliary body, zonule and lens infront***(Anthony et al., 1997)***.

Its rigidity and viscosity are produced by a delicate fibrillar meshwork which consists primarily of type II collagen that is intertwined with hyaluronic acid,

glycoprotein and proteoglycans***(Peymanand Schulman, 1994).***

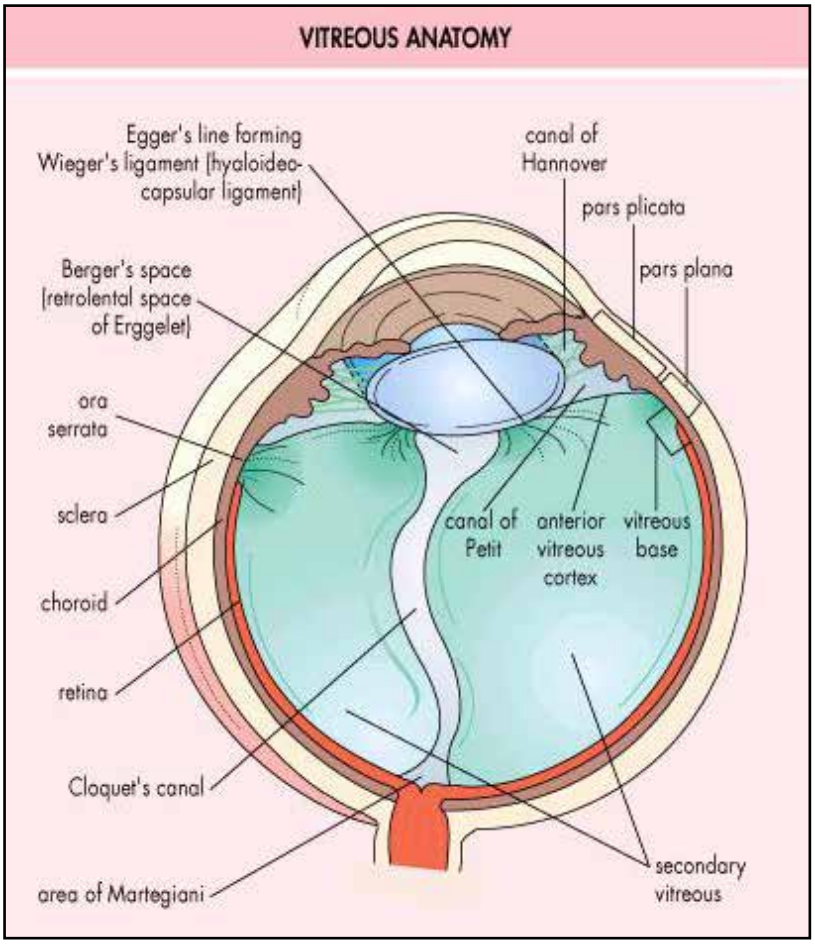


**Fig. (1):**Diagram of corpus vitreous ***(Schepensand Neetens, 1987).***

The vitreous body is roughly spherical.Its outer portion which is particularly denserthan the central vitreous is called the cortex and is approximately 100 µm in thickness. The term hyaloid membrane refers to the surface of the vitreous cortex. The vitreous cortex is divided into