

# **ENZYMATIC ASSISTED VITRECTOMY**

**Essay**

*Submitted for partial fulfillment of master  
degree in Ophthalmology*

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**2014**

بسم الله الرحمن الرحيم

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صدق الله العظيم  
سورة البقرة - الآية 32

## Table of contents

List of figures	II
List of tables	V
List of abbreviations	VI

Introduction	1
Aim of the work	4
Vitreous anatomy	5
Pathophysiology of the vitreous	17
Plasmin enzyme	26
Other enzymes used in enzymatic vitrectomy	84
English summary	115
References	119
Arabic summary	138

## List of figures

<i>Figure</i>	<i>Title</i>	<i>Page</i>
<i>1</i>	Diagram of corpus vitreous.	<i>6</i>
<i>2</i>	Arrangement of vitreous fibers.	<i>9</i>
<i>3</i>	Ultra structure of human posterior vitreous cortex.	<i>12</i>
<i>4</i>	Arrangement of vitreous fibers.	<i>13</i>
<i>5</i>	Dark field horizontal optical view of vitreous in old human.	<i>17</i>
<i>6</i>	Schematic representation of the fibrinolytic system or plasminogen / plasmin system.	<i>27</i>
<i>7</i>	Plasmin absorbance at 405 nm across time in seconds.	<i>32</i>
<i>8</i>	SEM of rabbit retinal surface after 30 minutes of injection.	<i>36</i>
<i>9</i>	SEM of eye injected with plasmin without vitrectomy.	<i>37</i>
<i>10</i>	Induction of PVD using tPA.	<i>38</i>
<i>11</i>	SEM showing the effect of cryopexy followed by BSS or tPA injection.	<i>39</i>
<i>12</i>	TEM images of the pig vitreoretinal interface.	<i>40</i>
<i>13</i>	SEM of plasmin treated eyes in different doses and different times of exposure.	<i>41</i>
<i>14</i>	SEM of the inner retinal surface from which the posterior vitreous cortex was completely detached and the smooth retinal surface after plasmin injection.	<i>42</i>
<i>15</i>	Transmission electronic microscope images of the eyes treated with plasmin and/or SF6.	<i>44</i>

16	SEM in eyes treated with vitrectomy alone.	46
17	SEM of plasmin treated eyes before vitrectomy.	46
18	The effect of 0.4 IU of autologous plasmin on macular hole.	56
19	OCT of macular hole closure after injection of plasmin enzyme.	57
20	Vitreomacular traction syndrome (VMT) before (A) and after (B) the injection of intravitreal plasmin.	61
21	Optical Coherence Tomography of the epiretinal membrane (MEM) before (A) and after (B) the Intravitreal injection of autologous plasmin.	61
22	(a) OCT scan before intravitreal APE injection (b) OCT scan 24 h after APE injection (c) 1 month and (d) 6 months after pars planavitrectomy.	62
23	Ocriplasmin: Truncated form of human plasmin.	67
24	Time to vitreomacular adhesion resolution following ocriplasmin injection.	81
25	Fundus photograph with severe inflammatory response and some fibrosis after injection of more than 1000 IU of urokinase.	86
26	SEM of normal vitreoretinal juncture vs. sensory retina after treatment with dispase.	90
27	Light micrograph of dispase treated eye.	93
28	SEM photomicrography of the retinal surface.	94

29	SEM of the inner retinal surface showing the effect of dispase and plasmin injection at deferent doses.	96
30	L.M Photomicrograph of vitreous and retina after injection of 20 IU of hyaluronidase in rabbit eye.	100
31	SEM of eyes injected with BSS vs. hyaluronidase.	101

## List of Tables

<i>Table</i>	<i>Title</i>	<i>Page</i>
<i>1</i>	Summary of experimental studies in the area of pharmacologic vitreolysis and posterior vitreous detachment	48
<i>2</i>	Key patient characteristics and design details of the two phase III trials of ocriplasmin in VMA	75
<i>3</i>	Efficacy of ocriplasmin in patients with symptomatic VMA	76
<i>4</i>	Ocular adverse events of ocriplasmin	78
<i>5</i>	Ocular adverse events following injection in numbers	82

## List of Abbreviations

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



<b>MW</b>	Molecular weight
<b>OCT</b>	Optical coherence tomography
<b>PAS</b>	Periodic acid Schiff
<b>PBS</b>	Phosphate buffered saline
<b>PDR</b>	Proliferative diabetic retinopathy
<b>PNLs</b>	Polymorphneuclear leukocytes
<b>PVD</b>	Posterior vitreous detachment
<b>PVR</b>	Proliferative vitreoretinopathy
<b>RD</b>	Retinal detachment
<b>r-Lys-Plg</b>	Recombinant lysine plasminogen
<b>r-mPlg</b>	Recombinant microplasminogen
<b>ROP</b>	Retinopathy of prematurity
<b>RPE</b>	Retinal pigment epithelium
<b>RRD</b>	Rhegmatogenous retinal detachment
<b>r-SK</b>	Recombinant streptokinase
<b>r-UK</b>	Recombinant urokinase
<b>RVO</b>	Retinal vein occlusion
<b>SDOCT</b>	Spectral domain optical coherence tomography
<b>SEM</b>	Scanning electron microscopy
<b>Ser<sup>741</sup></b>	Serine amino acid
<b>SF6</b>	Sulphar hexafluoride
<b>TA</b>	Triamcinolone acetonide
<b>TEM</b>	Transmission electron microscopy
<b>TG-MV-006</b>	Code name of the study
<b>TG-MV-007</b>	Code name of the study
<b>tPA</b>	Tissue plasminogen activator
<b>UK</b>	Urokinase
<b>UKr</b>	Urokinase receptor
<b>VA</b>	Visual acuity
<b>Val<sup>562</sup></b>	Valine amino acid
<b>VMA</b>	Vitreomacular adhesion
<b>VMT</b>	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 in vitreous surgery, because the mechanical creation of PVD often leads to complications (*Akiba et al., 1990*).

Vitreo-retinal surgical procedures are 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**

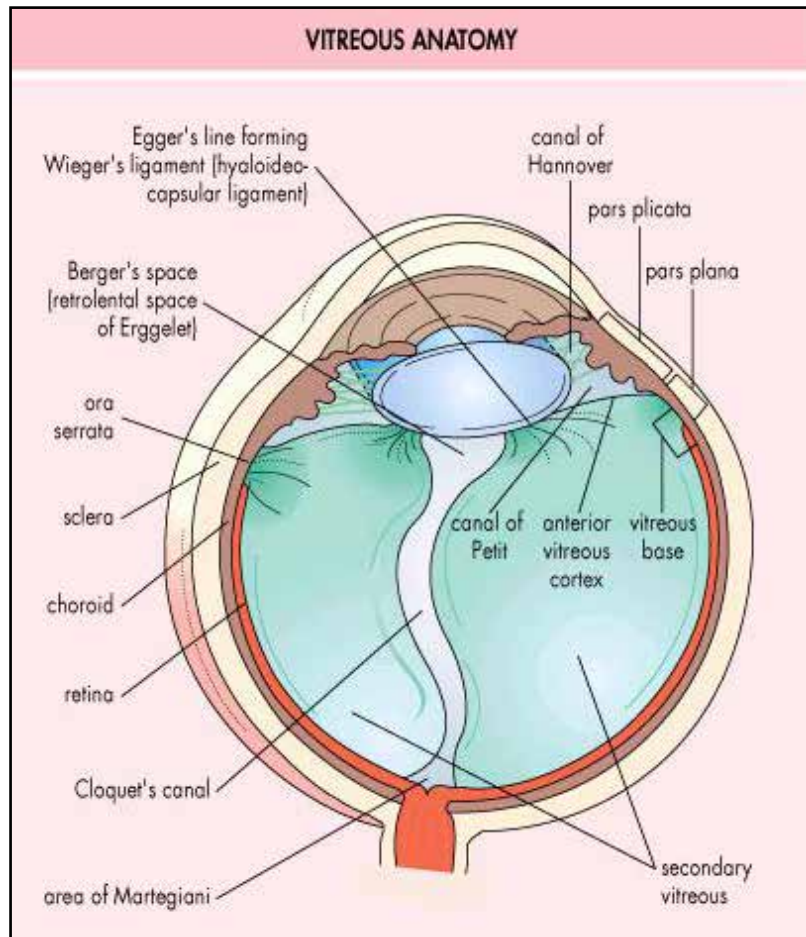
### **Macroscopic structure of the vitreous**

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. It is 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 in front(*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 denser than the central vitreous is called the cortex and is approximately 100  $\mu\text{m}$  in thickness. The term hyaloid membrane refers to the surface of the vitreous cortex. The vitreous cortex is divided into