GEN KÖK
Genom ve Kök Hücre Merkezi
Genome and Stem Cell Center

KURU TİP YBMD'DE

KÖK HÜCRE TEDAVİSİ

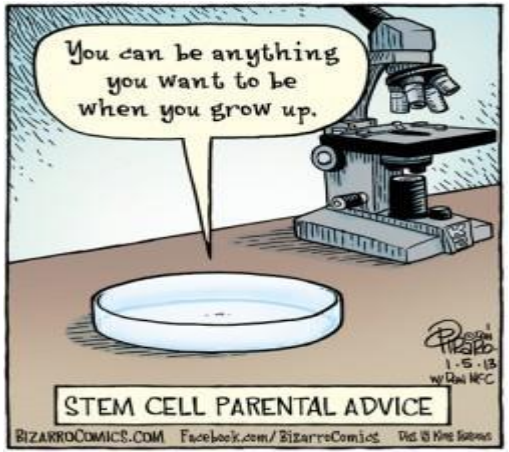
Prof.Dr. Ayşe Öner, FEBO
Erciyes Universitesi Tıp Fakültesi
Göz Hastalıkları AD KAYSERİ
ANKARA

ERCİYES ÜNİVERSİTESİ
1978

KÖK HÜCRE NEDİR?

Kök Hücre:

* Hücrenin özelleşmemiş en temel ve saf halidir.
* Vücuttaki pek çok hücre tipine differensiye olabilir.
* Hasarlı hücre ve dokuları onarabilir.



KÖK HÜCRELERİN ÖZELLİKLERİ

- Proliferasyon
- Self-renewal: Kendini yenileme
- Differensiasyon

DİFFERENSİASYON

Differensiasyon: Farklı hücrelere dönüşebilir.

Bu süreçte internal ve eksternal faktörler rol alır.

İnternal faktörler: Hücrenin genleriyle ilişkilidir.

Eksternal faktörler hücrenin bulunduğu ortamdaki diğer hücreler ve moleküllerle (microenvironment) ilişkilidir..

KÖK HÜCRE TİPLERİ

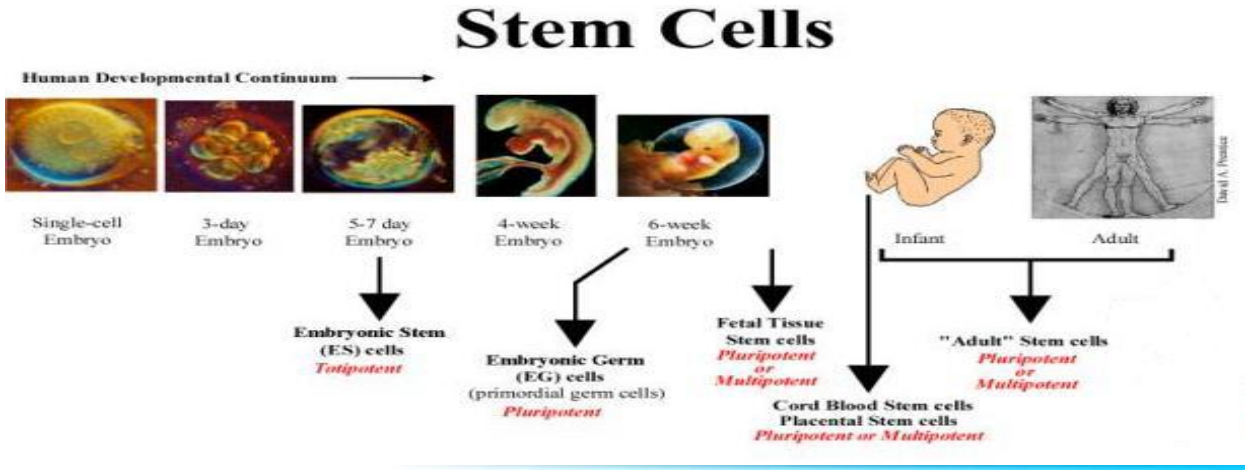
1-EMBRYONİK KÖK HÜCRE

2- ERİŞKİN KÖK HÜCRE

- Mesenkimal KH
- İndüklenmiş pluripotent KH

3-KORDON KANI KÖK HÜCRESİ

4- AMNİOTİK SIVI KÖK HÜCRESİ



ÜLKEMİZDE KÖK HÜCRE UYGULAMALARI

* İnsan embriyonik kök hücre kullanımı yasaktır (2005)

* Erişkin kök hücre ve İPKH kullanımı için ise Lokal Etik Kurumdan ve Sağlık Bakanlığı'ndan (Doku ve Organ Nakli Biriminden) onay gereklidir.

(TCK: 90)

KÖK HÜCRE TEDAVİSİNİN MEKANİZMASI

* (1) Hücre Replasmanı: Sağlıklı kök hücreler dejenere hücrelerin yerini alabilir (Differensiasyon).

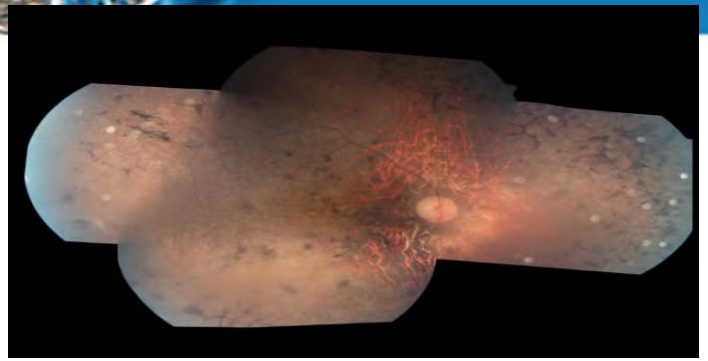
* (2) Nutrisyonel Destek: Sağlıklı kök hücreler salgıladıkları faktörlerle etraftaki hücrelerin yaşamlarını desteklerler.
  (bFGF, VEGF, M-CSF, GM-CSF, PlGF, TGF-β, HGF, IGF-1, IL, angiogenin)

* (3) Yeni bağlantılar oluştururlar.

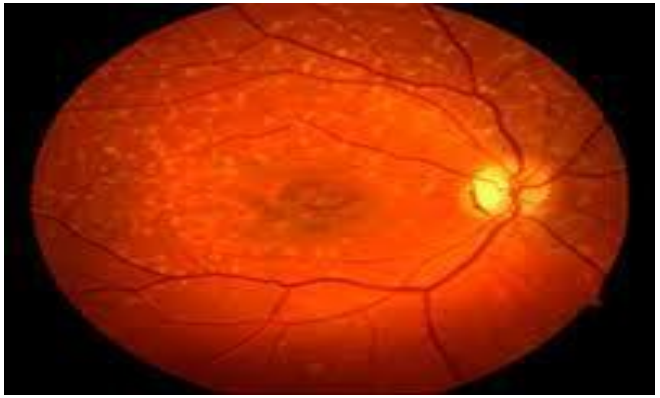
Gözde Kök Hücre Kullanımı

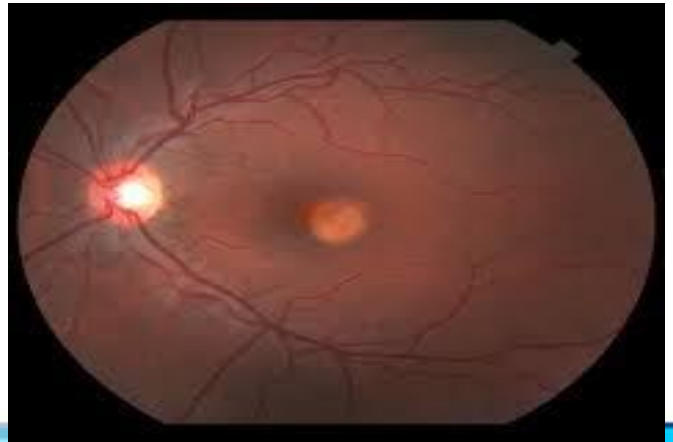
* Çok küçük dozlar yeterli olur.
* Cerrahi yaklaşım kolaydır.
* Nakledilen hücre kolayca izlenir.
* Gözün immün yapısı uygundur.
* Diğer göz kontrol olarak kullanılabilir.
* Ekstraoküler yayılım söz konusu değildir.

HEDEFLENEN RETİNAL HASTALIKLAR



RP, Leber KA, YBMD, BEST, STARGARDTS’





*YBMD’DE KLİNİK ÇALIŞMALAR

EKH ÇALIŞMALARI

* Faz ½: Subretinal EKH
* 9 **Stargardt's MD** ve 9 kuru tip **YBMD** olgusu
* 22 ay takip
* Ciddi yan etki yok
* 13 (72%) olguda subretinal pigmentasyon artışı
* 10 olguda EİDGK artışı
* Görme ile ilgili hayat kalitesinde artış.

* Schwartz SD et al. Human embryonic stem cell-derived retinal pigment epithelium in patients with age-related macular degeneration and Stargardt's macular dystrophy: follow-up of two open-label phase 1/2 studies. Lancet. 2015 Feb 7;385(9967):509-16.

EKH ÇALIŞMALARI

Stem Cell Reports
Article

ISSCR

OPEN ACCESS

Treatment of Macular Degeneration Using Embryonic Stem Cell-Derived Retinal Pigment Epithelium: Preliminary Results in Asian Patients

Won Kyung Song,[1,*] Kyung-Mi Park,[2] Hyun-Ju Kim,[2] Jae Ho Lee,[3] Jinjung Choi,[4] So Young Chong,[5] Sung Han Shim,[6] Lucian V. Del Priore,[7] and Robert Lanza[8,*]
[1]Department of Ophthalmology, CHA Bundang Medical Center, CHA University, Seongnam-si, Gyeonggi-do 463-712, Republic of Korea

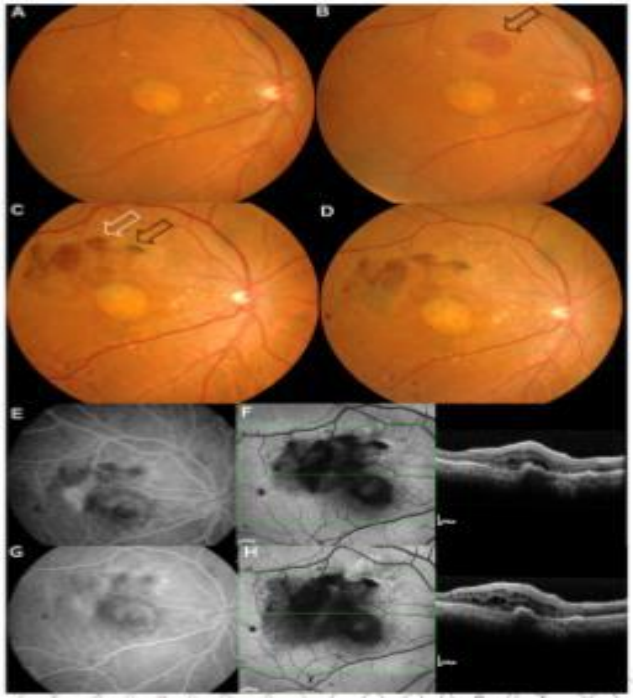
4 YBMD, 4 Stargardt MD olgusu, 1 yıllık takip

Ciddi okuler ve sistemik yan etki yok

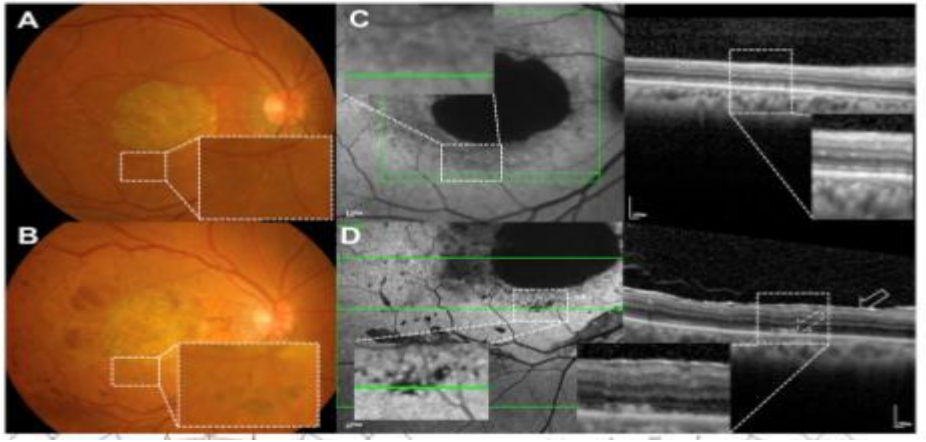
1 olguda KNVM ve 3 doz Lucentis

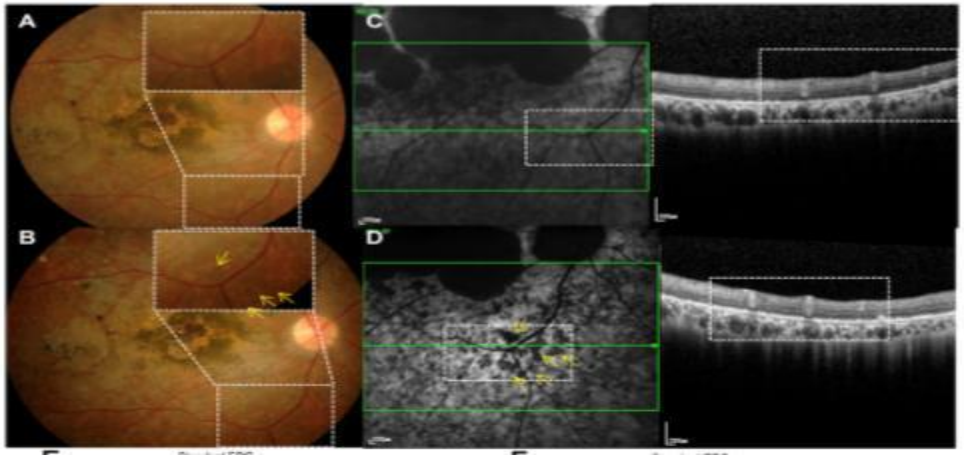
Tüm olgularda pigmentasyon artışı

Tüm olgularda GK artışı



KNVM





Subretinal pigmentasyon

www.impactjournals.com/oncotarget/ Oncotarget, Vol. 7, No. 30

Research Paper: Gerotarget (Focus on Aging)

Cell surgery and growth factors in dry age-related macular degeneration: visual prognosis and morphological study

Paolo Giuseppe Limoli[1], Celeste Limoli[1], Enzo Maria Vingolo[2], Sergio Zaccaria Scalinci[3] and Marcella Nebbioso[4]

J Vis Exp. 2018 Feb 12;(132). doi: 10.3791/56469.

Regenerative Therapy by Suprachoroidal Cell Autograft in Dry Age-related Macular Degeneration: Preliminary In Vivo Report.

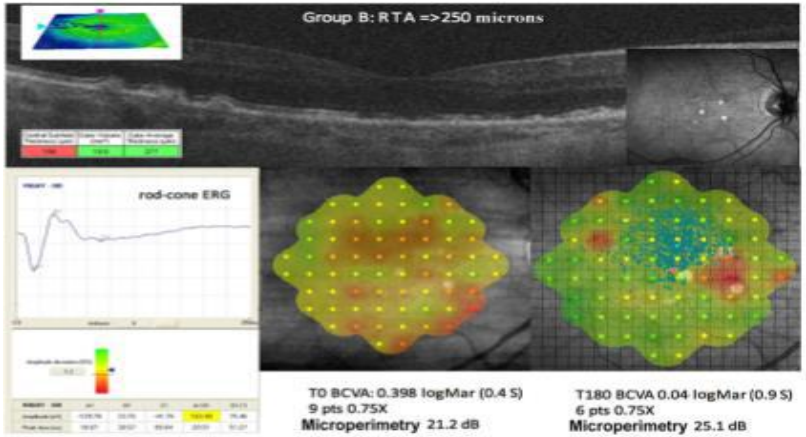
Limoli PG[1], Vingolo EM[2], Limoli C[1], Scalinci SZ[3], Nebbioso M[4].

25 OLGUNUN 36 GÖZÜ
KURU TİP YBMD
SUPRAKOROİDAL ADMKH

Table 3: Patient compliance analysis (PCA) shows that, at 6 months post surgery, 19 of 36 eyes (52.78%) recorded better vision, 14 (38.89%) no change in functional situation, and 3 (8.33%) a worsening.

PCA	Group A	Group B	Total
Number of eyes	14	22	36
Improved (%)	5 (35.71)	14 (63.64)	19 (52.78)
Unchanged (%)	7 (50)	7 (31.82)	14 (38.89)
Worse (%)	2 (14.29)	1 (4.55)	3 (8.33)

Among the 19 eyes of patients who noted an improvement at 6 months post surgery, 5 (26.3%) belong to group A and 14 (73.7%) to group B.



Mikroperimetri örneği

• Clinical Research •

Evaluating role of bone marrow-derived stem cells in dry age-related macular degeneration using multifocal electroretinogram and fundus autofluorescence imaging

Atul Kumar[1], Neha Midha[1], Sujata Mohanty[2], Annu Chohan[1], Tulika Seth[3], Varun Gogia[1], Shikha Gupta[1]

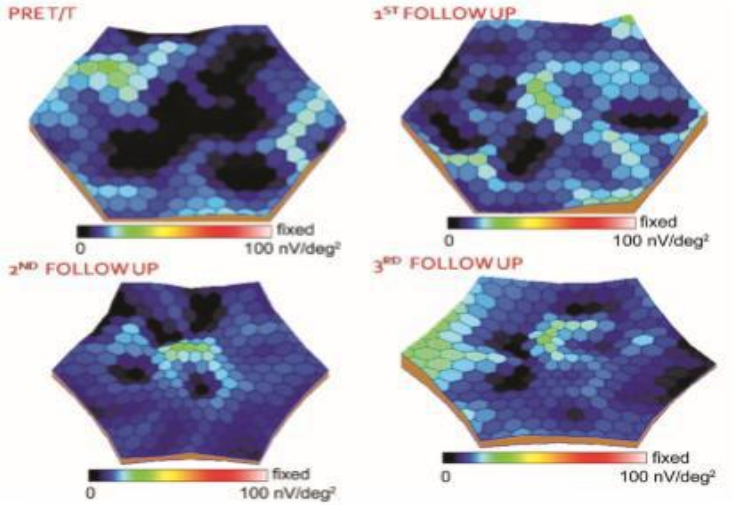
30 hasta, santral GA olan olgular, GK 0.1 den düşük olanlar

Kötü olan göze otolog Kİ- MKH

6 aylık takip, Mf ERG de iyileşme

GA boyutunda küçülme (Diğer gözde büyüme)

GK'de fark yok (Diğer gözde azalma)



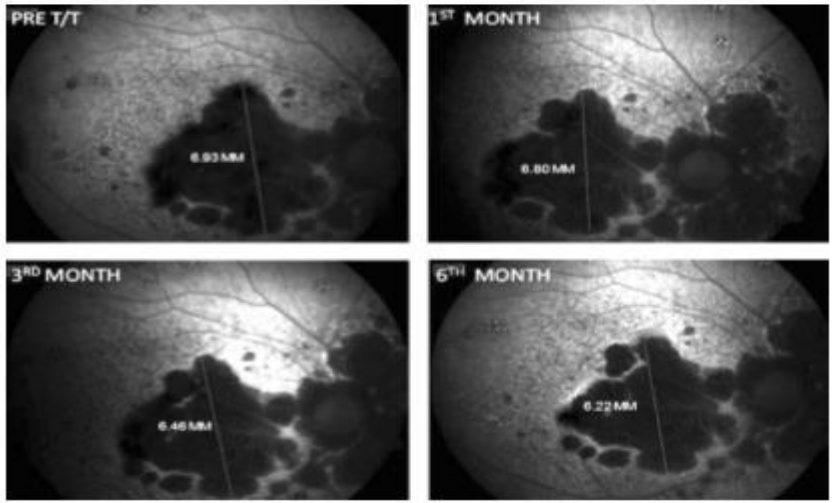
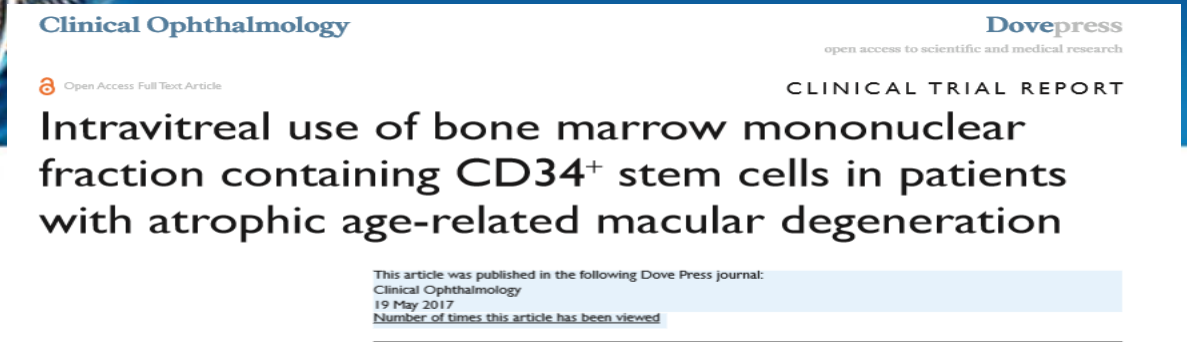


Figure 4 Representative FAF imaging of a patient prior to stem cell injection and on three subsequent follow-ups after the injection.

Mf ERG ve FAF örneği



Clinical Ophthalmology

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CLINICAL TRIAL REPORT

Intravitreal use of bone marrow mononuclear fraction containing CD34+ stem cells in patients with atrophic age-related macular degeneration

This article was published in the following Dove Press journal:
Clinical Ophthalmology
19 May 2017
Number of times this article has been viewed

10 ATROFİK YBMD, GK 20/100 DEN DÜŞÜK OLGULAR

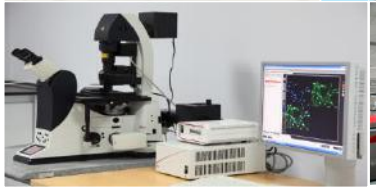
OTOLOG Kİ-MKH, İNTRAVİTREAL

GK ‘ DE ANLAMLI ARTIŞ (20/320 DEN 20/200’E YÜKSELMİŞ)

PERİMETRİDE İYİLEŞME

ATROFİK ALANLARDA KÜÇÜLME

EÜTF VE GENKÖK



FAZ II ÇALIŞMAMIZ

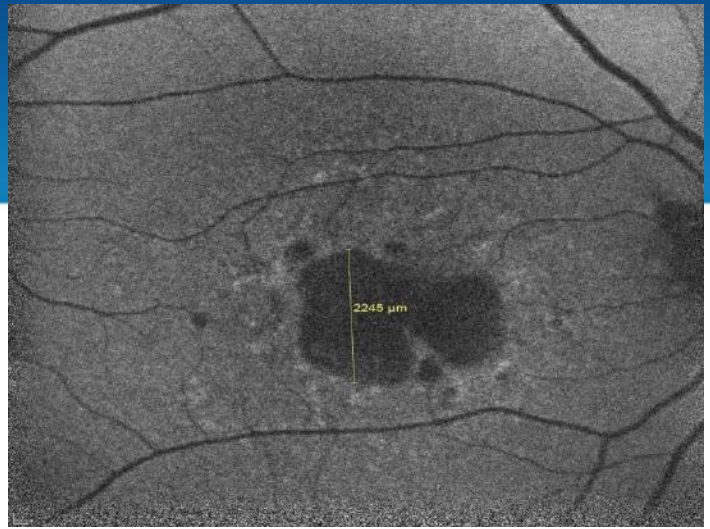
* 20 olgu opere edildi. (4 YBMD OLGUSU)
* En iyi gören olgumuz 1 mps
* Görmesi düşük olan göz opere edildi.
* Suprakoroidal olarak adipoz dokudan derive edilmiş allojenik mezenkimal KH kullanıldı.

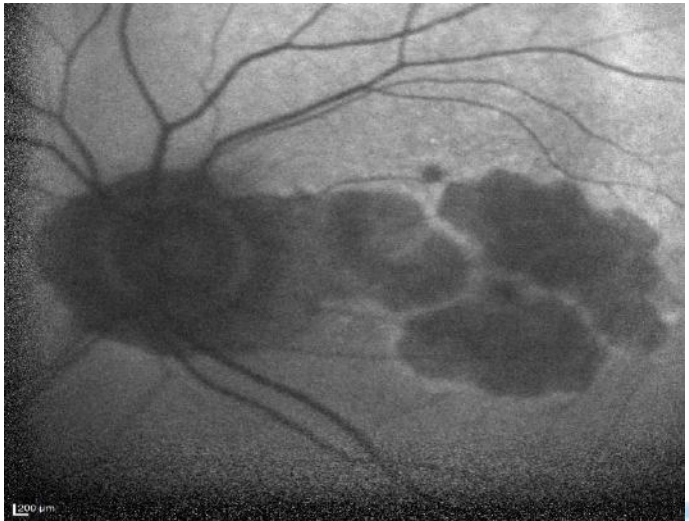
GMP (Good manufacturing practice) (İyi Klinik Uygulamalar)

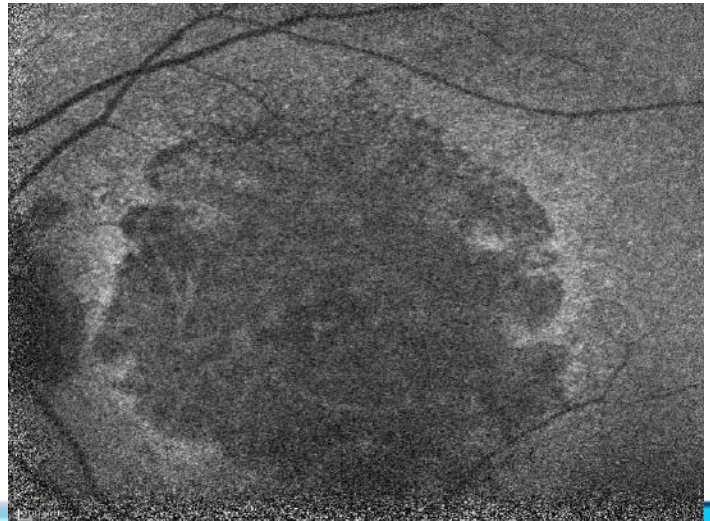
ADMKH ler uluslar arası standartlarda üretildi

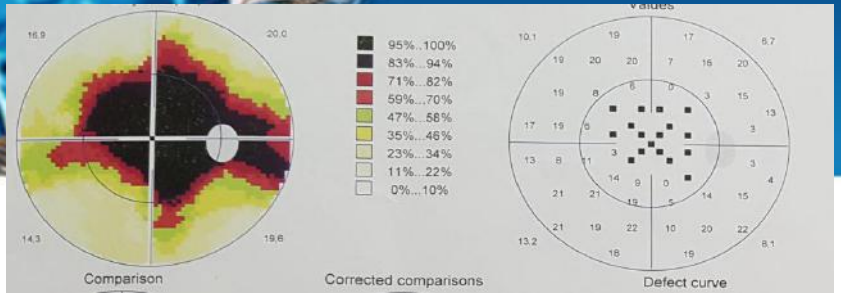
SONUÇLAR

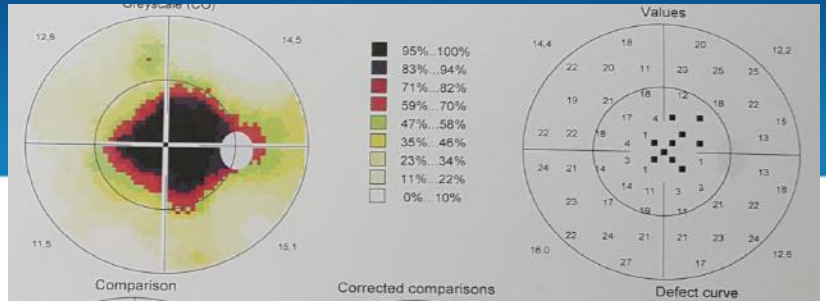
* Hiçbir olguda sistemik komplikasyon olmadı.
* Hiçbir olguda okuler komplikasyon yok.
* Postop konjonktival hiperemi dışında olumsuz bulgu yok
* Reaksiyon yok

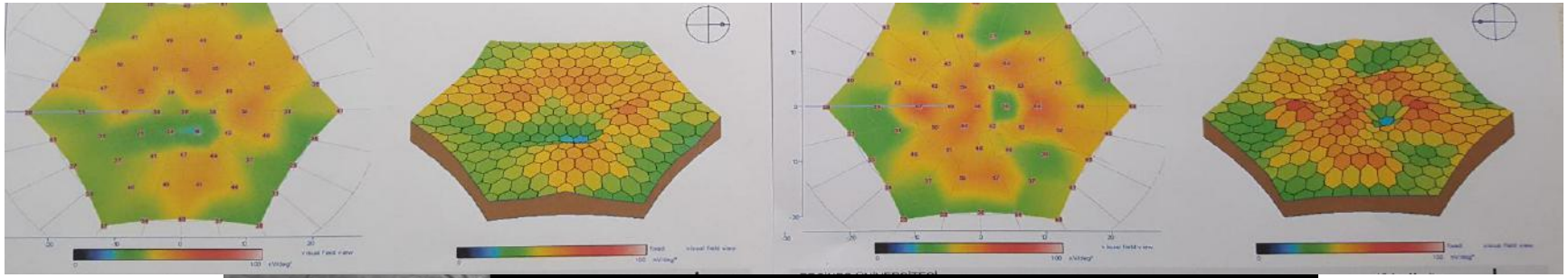

2245 µm

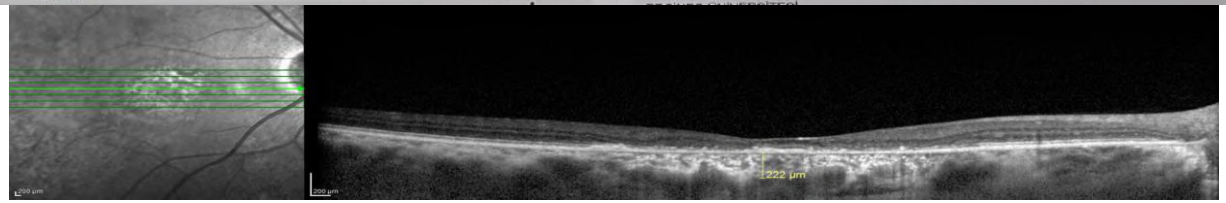

200 µm

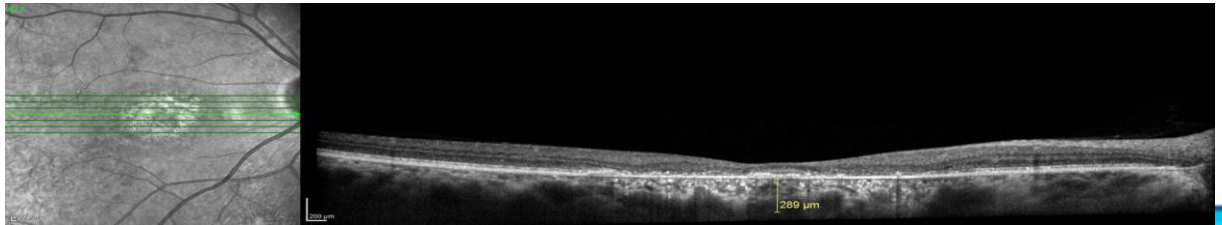


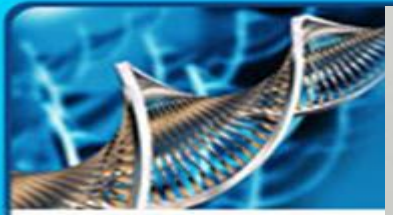

95%..100%
83%...94%
71%...82%
59%...70%
47%...58%
35%...46%
23%...34%
11%...22%
0%...10%
Comparison
Corrected comparisons
Defect curve

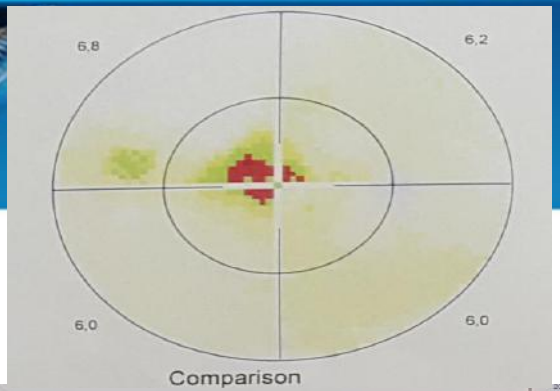

95%..100%
83%...94%
71%...82%
59%...70%
47%...58%
35%...46%
23%...34%
11%...22%
0%...10%
Comparison
Corrected comparisons
Defect curve

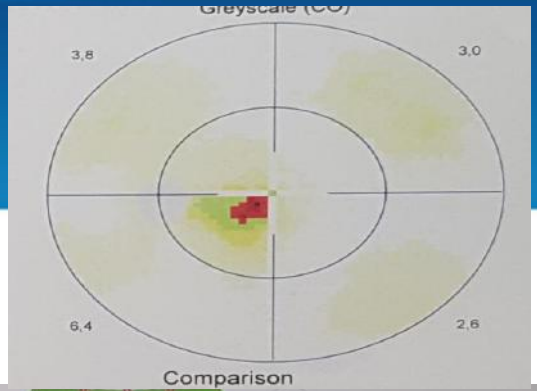


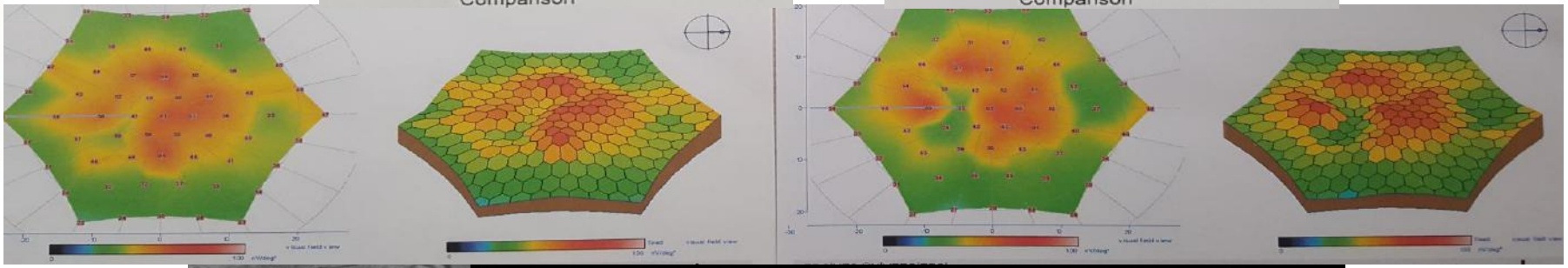

222 µm

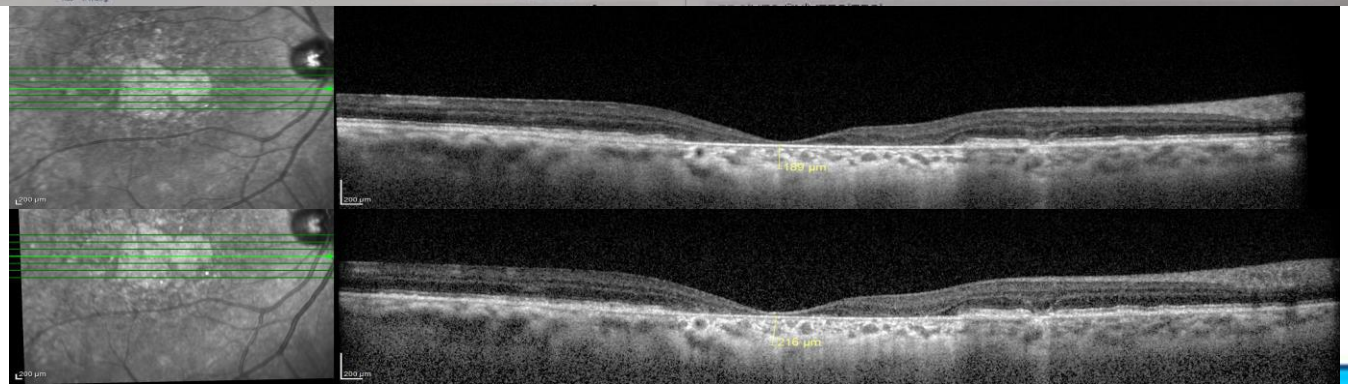

289 µm

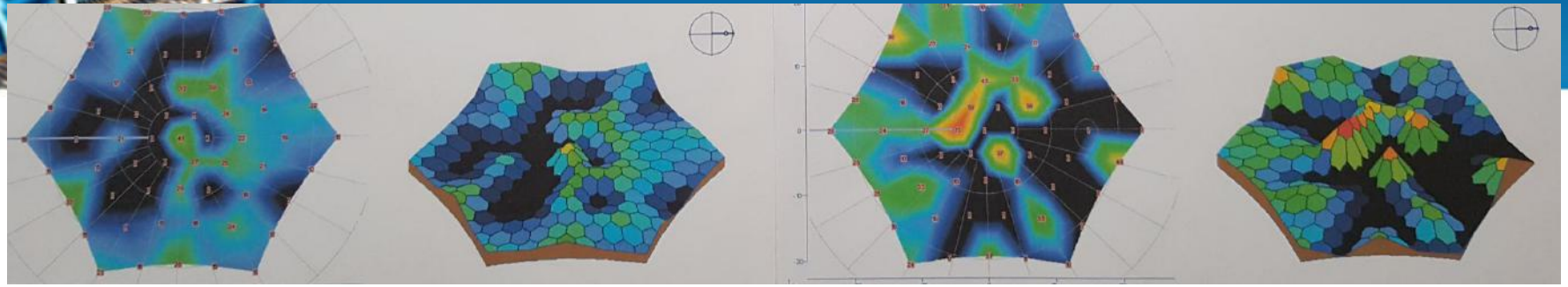


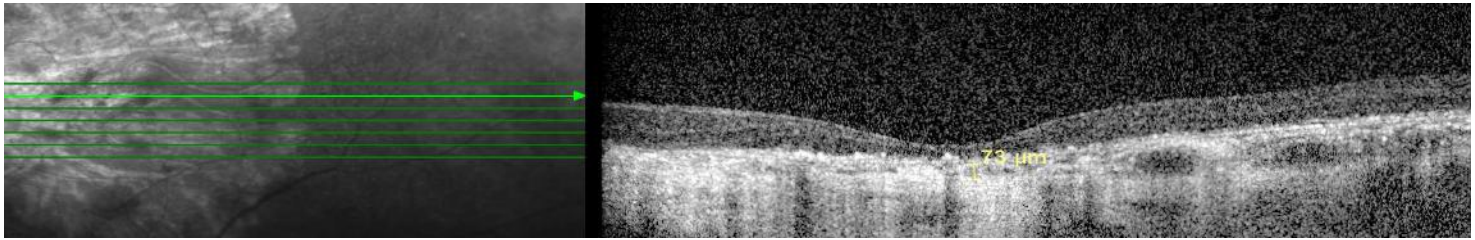

6,8
6,2
6,0
6,0
Comparison

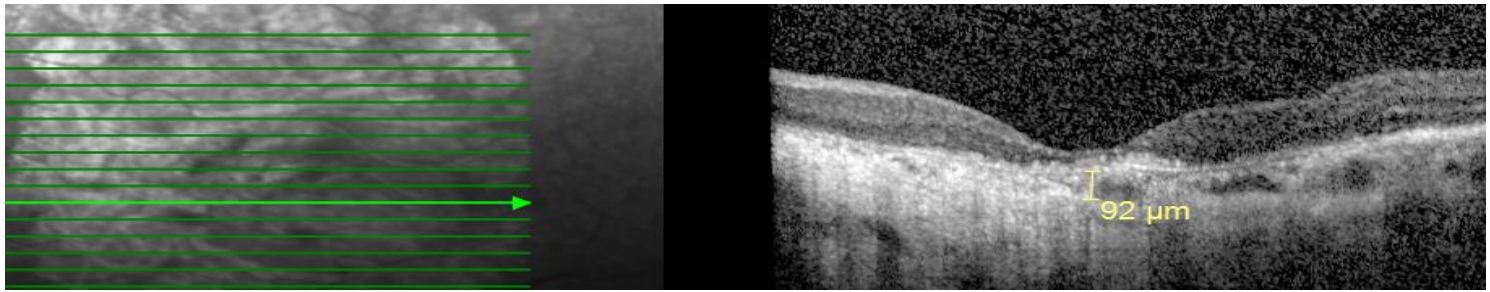

Greyscale (CO)
3,8
3,0
6,4
2,6
Comparison

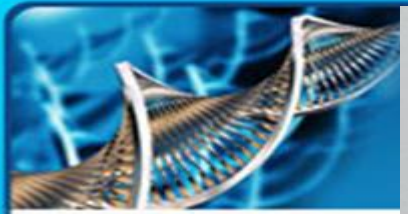


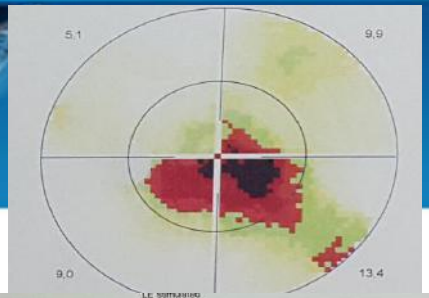


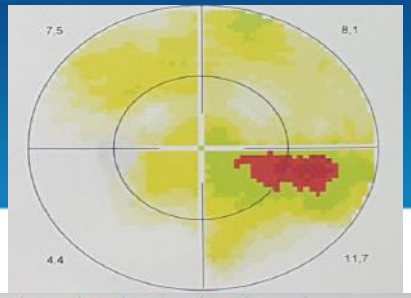


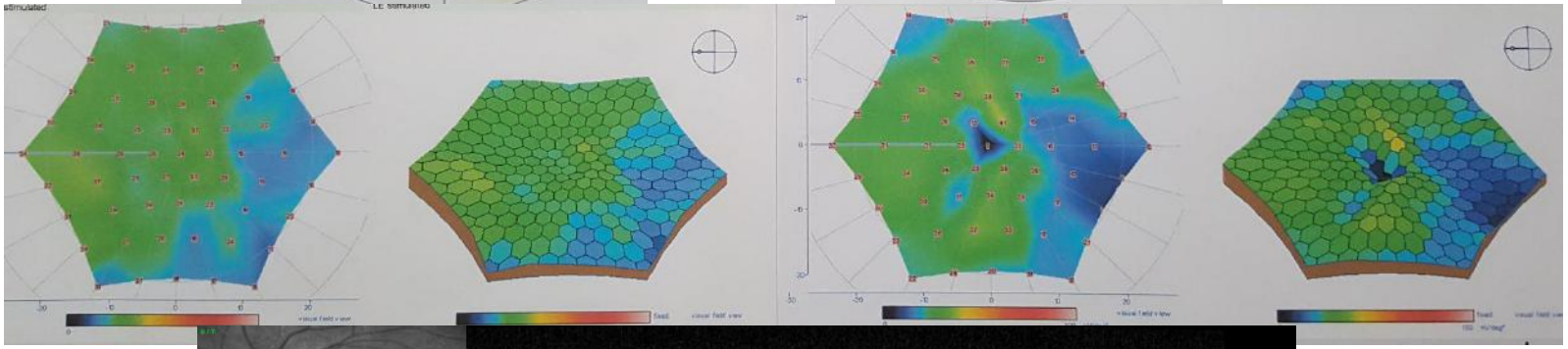

73 µm

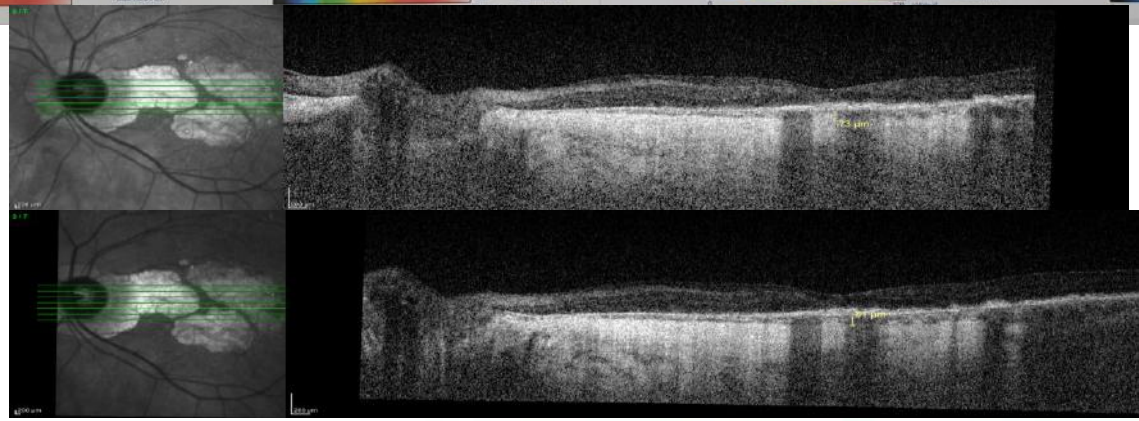

92 µm




5,1
9,9
9,0
13,4


7,5
8,1
4,4
11,7





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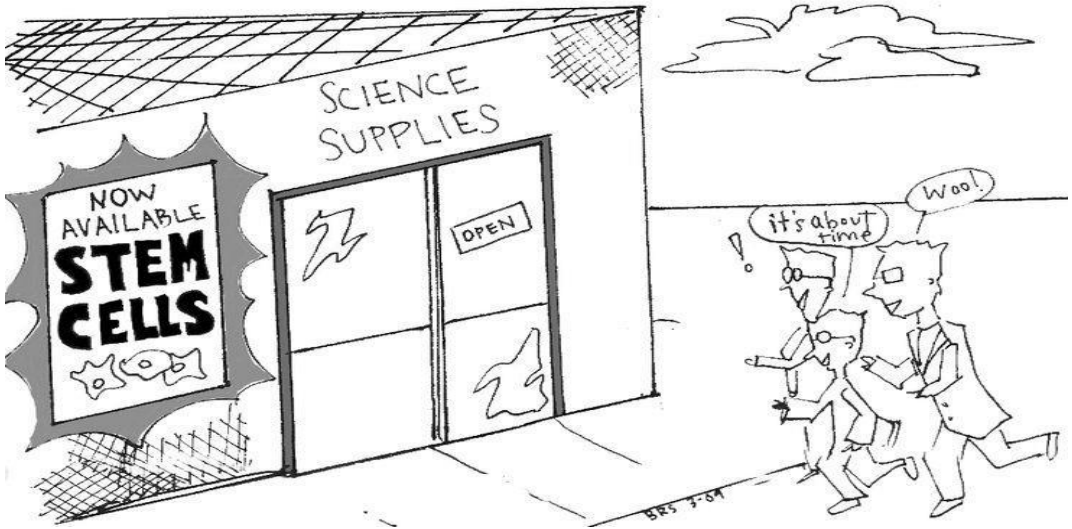
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STEM CELLS
OPEN
it's about time
Woo!