

**Critical**

health



**Retmarker**

## Introduction

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## Contents

Corporate

Scientific R&D

Retmarker Products

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Corporate

Scientific R&D

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## Hello, we are Critical Health



- Spin-off from Critical Software, incorporating health care projects started in 2005.
- Certified Medical Device Manufacturer (93/42/EEC Annex II.3) providing software solutions focusing on preventing loss of vision, mobility and cognitive skills in an aging population.
- Business model based on partnerships with internationally recognized Scientific Institutes.

# Rock solid reliability



- Critical Software is a successful European IT services company, **certified CMMI level 5**.
- Provides business and mission critical systems for defense, aerospace, telecommunications, etc.
- Founded in 1998, has 300+ employees across 5 countries, generating ~20M€ in revenue.
- Successfully spun off product companies.
- Clients are some of the most demanding companies in the world.



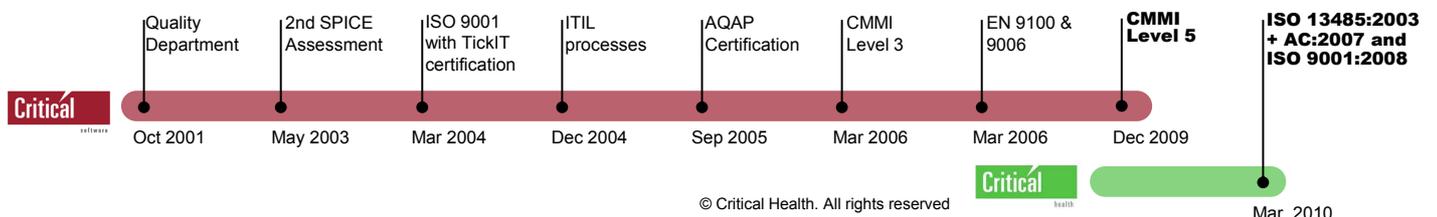
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# Quality is in our DNA

- Critical Software's QMS is in accordance with ISO 9001:2008 standard using the TickIT scheme.
- **CMMI level 5**, the most prestigious software engineering Quality certification, offered by the SEI.



- Critical Health's QMS is certified according to ISO 13485:2003+AC:2007 and ISO 9001:2008.



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Mar 2010

# Vision and Value Proposition



## Vision

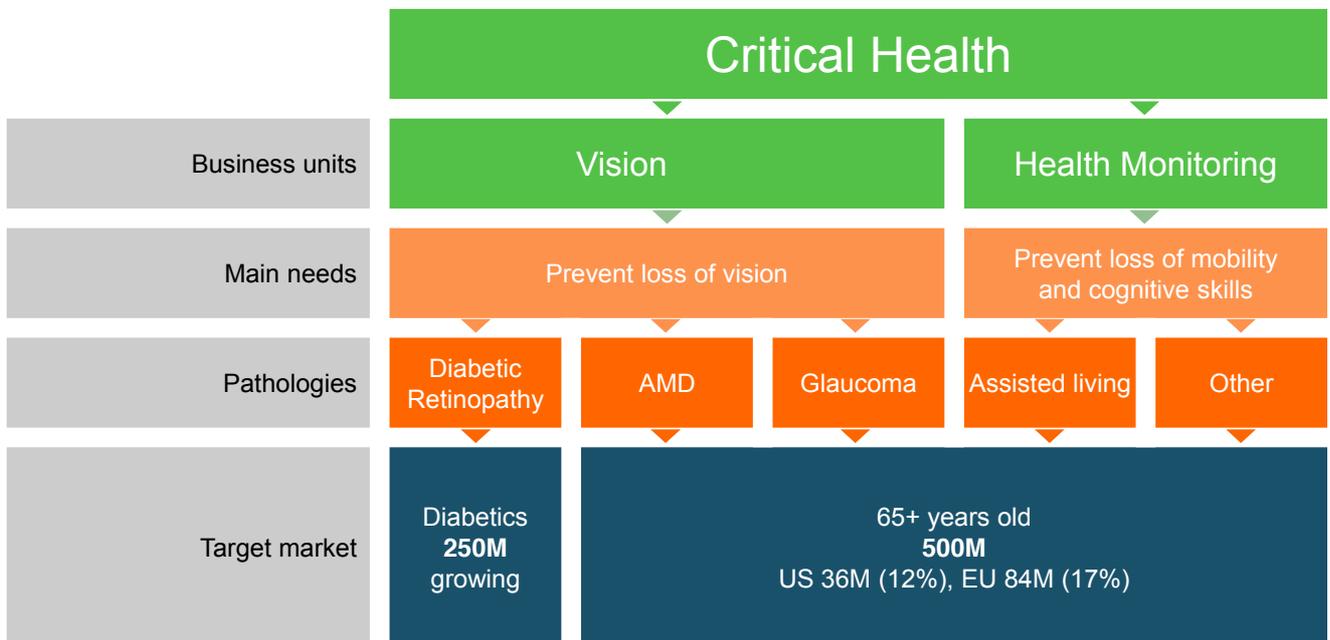
To improve the Quality of Life and reduce total Healthcare Spending.

## Value Proposition

To provide critical Health Information to everyone through the marketing of innovative and accessible products.

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# Our strategic Business Units



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# Vision

**Regulatory:**



TÜV Rheinland  
Precisely Right.

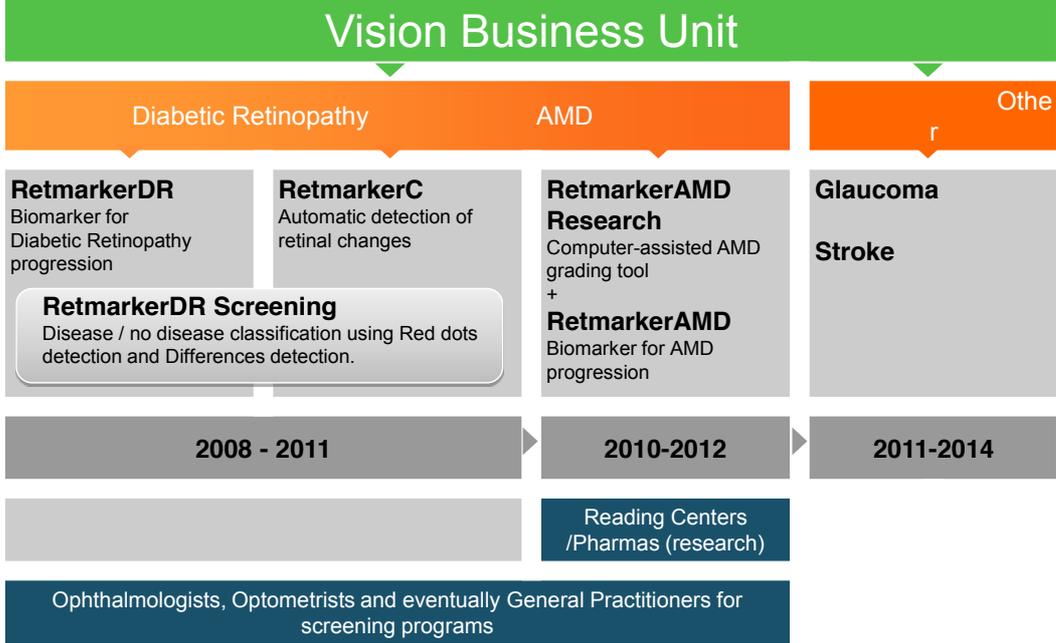
**Awards:**



**Intellectual Property:**

**U.S. Patent No. 7,856,135**  
+ another patent pending

# Roadmap



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## AIBILI, our scientific partner



Retmarker products were developed in partnership with AIBILI.

- AIBILI is an internationally renowned Scientific Institute, led by Professor Cunha-Vaz.
- AIBILI is the main responsible for the scientific validation of the technology used in Retmarker.
- AIBILI is a Research Technology Organization (RTO) dedicated to help the development of new products for health imaging, pharmaceutical and biotechnology companies.
- AIBILI is certified by NP EN ISO 9001:2008

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## AIBILI, our scientific partner



AIBILI develops:

- New tools for Diagnostic Imaging.
- Fluorescence measurement "in vivo".

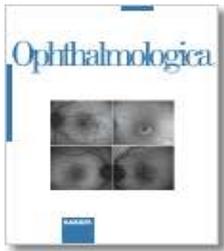
AIBILI performs:

- Clinical Trials in DR, AMD, Glaucoma.
- Bioavailability Studies in Physical-Chemical Testing.
- Technology Transfer.
- Scientific information to support decision making in healthcare policy and practice.

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# Scientific evidence

AIBILI has been presenting research related to RetmarkerDR and RetmarkerC's underlying concepts at important scientific forums.



- Scientific papers supporting RetmarkerDR technology were published by Ophthalmologica.

The main conclusions of these studies are:

- MA turnover (more than just MA count) is a key indicator for the development of Diabetic Retinopathy (DR).
- MA tracker\* is a reliable software tool which can be used to capture the MA turnover in the initial stages of DR.

\* MA tracker is the base algorithm that was used in the development of RetmarkerDR

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# New Results corroborate findings

Professor Michael Ulbig, University Eye Hospital of the Ludwig Maximilians University, Germany will present in Main Session 09, Saturday, 28th, 14h00

## MA Turnover as a predictor of CSME development

Results obtained are in line with AIBILI published study but with bigger dataset.

### Population

- A group of 290 eyes was analyzed (CALDIRET study)
- 5 year follow-up by fundus photography

### Results

Formation Rate	CSME		No CSME	
[6,∞[	14	28,6%	22	9,1%
[5-6[	1	2,0%	7	2,9%
[4-5[	3	6,1%	6	2,5%
[3-4[	6	12,2%	9	3,7%
[2-3[	11	22,4%	24	10,0%
[1-2[	7	14,3%	56	23,2%
[0-1[	7	14,3%	117	48,5%
<b>Total</b>	<b>49</b>		<b>241</b>	
"True"	71,4%		71,8%	

### Images

- Initially captured in film and stored as slides that were scanned
- Three images used per patient, for visits at baseline, after 6 month and after one year

### Statistical Indicators

- True Positives: 71,4%
- True Negatives: 71,8%
- Negative Predictive Value: 92,51%
- Odds Ratio: 6,36

"True" refers to eyes that developed CSME and had a high MA Formation Rate, or eyes that did not develop CSME and had a low MA Formation Rate

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## Behind Retmarker...

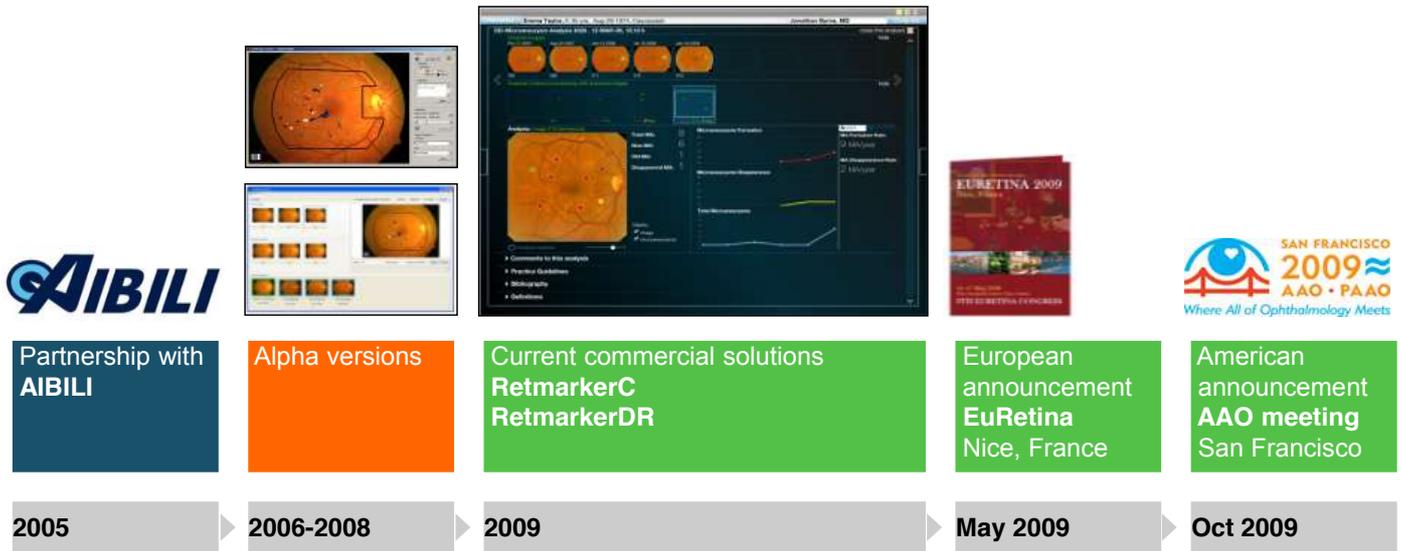


Retinal diseases, such as Diabetic Retinopathy (DR), Glaucoma and Age-related Macular Degeneration (AMD), are the leading causes of vision loss in the Western World.

**Early detection** and treatment of retinal diseases is critical!

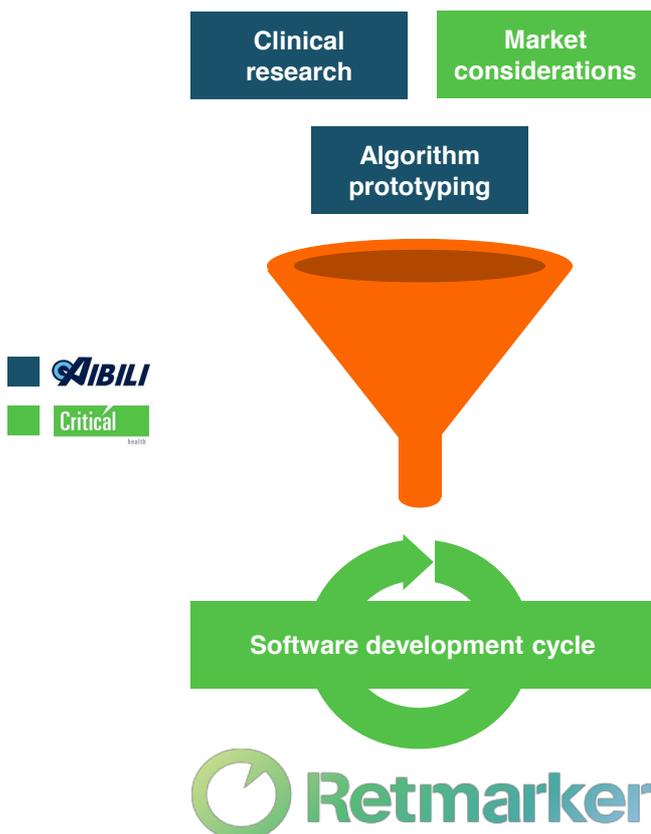
As they evolve over time, it is required close monitoring in order to support the best disease management options.

# From prototype to product



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## Retmarker's Development



- Special focus on user interaction and feedback, aimed for an high level of usability for both experienced and casual users.
- State-of-the-Art UI, developed using Microsoft's Windows Presentation Foundation.

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# Product portfolio

Regulatory:



TÜVRheinland  
Precisely Right.

Awards:



Intellectual Property:

**U.S. Patent No. 7,856,135**  
+ another patent pending

## Product Promise / Value Proposition



Automatic detection of retinal changes over time.



Biomarker for Diabetic Retinopathy progression



Computer-assisted AMD grading tool

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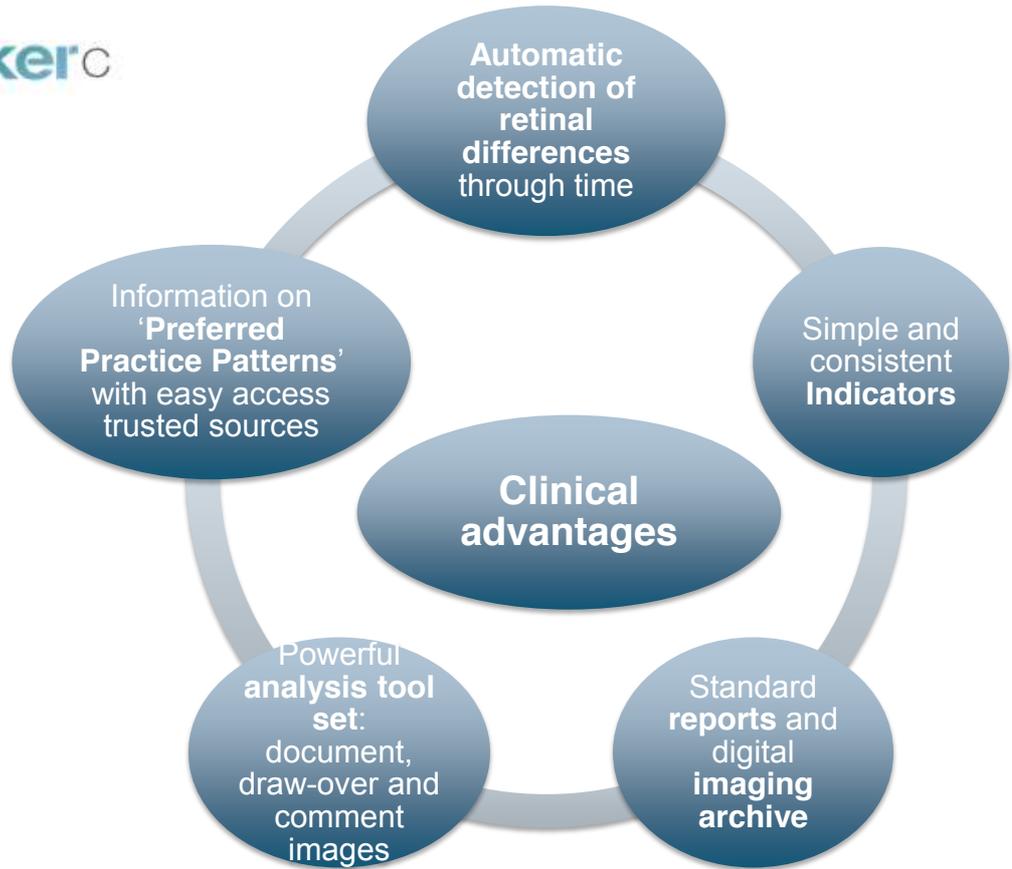
The image displays two overlapping screenshots of the Retmarker software interface. The left screenshot shows the 'Image Differences Analysis' for patient Emma Taylor, with a timeline of retinal fundus images from 2007 to 2009. The right screenshot shows the 'Microaneurysm Analysis' for the same patient, displaying a list of detected microaneurysms (MA) and a graph of 'Microaneurysms Formation' and 'Microaneurysms Disappearance' over time. The graph shows a total of 8 MAs, with 6 new, 1 old, and 1 disappeared. The formation rate is 9 MA/year and the disappearance rate is 2 MA/year.



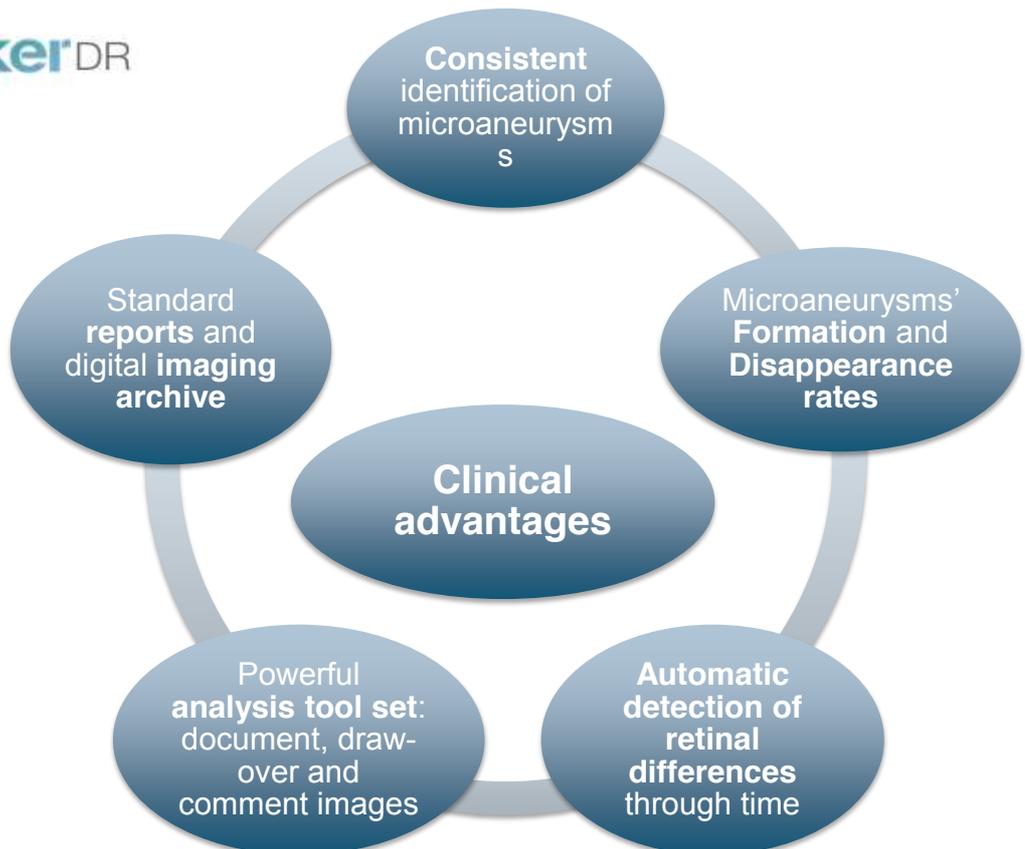
Automatic detection of retinal changes



Biomarker for Diabetic Retinopathy progression



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# Technical Requirements



## Minimum Hardware Requirements

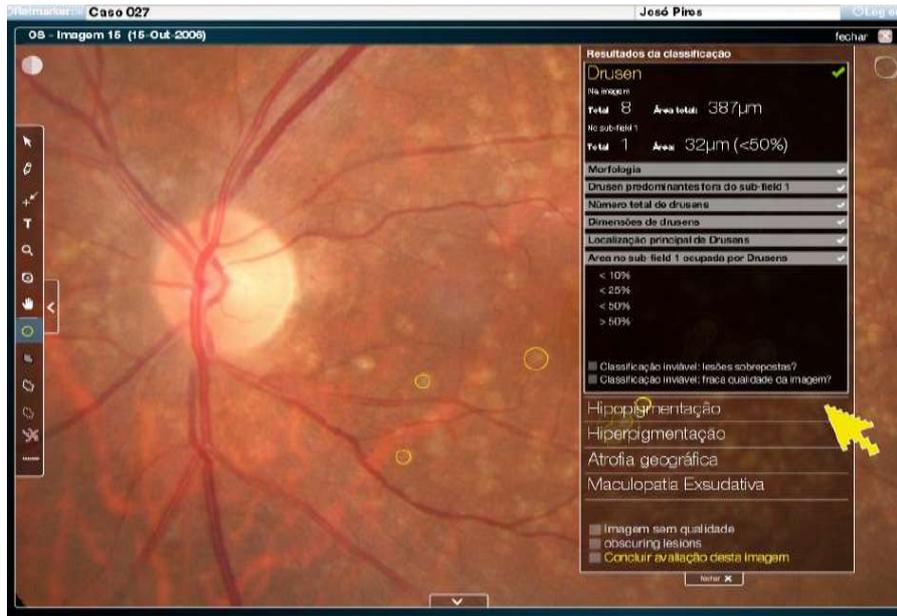
- Intel Pentium 2.0 GHz or compatible
- 1Gb RAM memory (2Gb recommended)
- 1024x768px graphics card
- 10Gb free Hard Disk space (20Gb recommended due to the image database)
- Mouse and keyboard

## Software Requirements

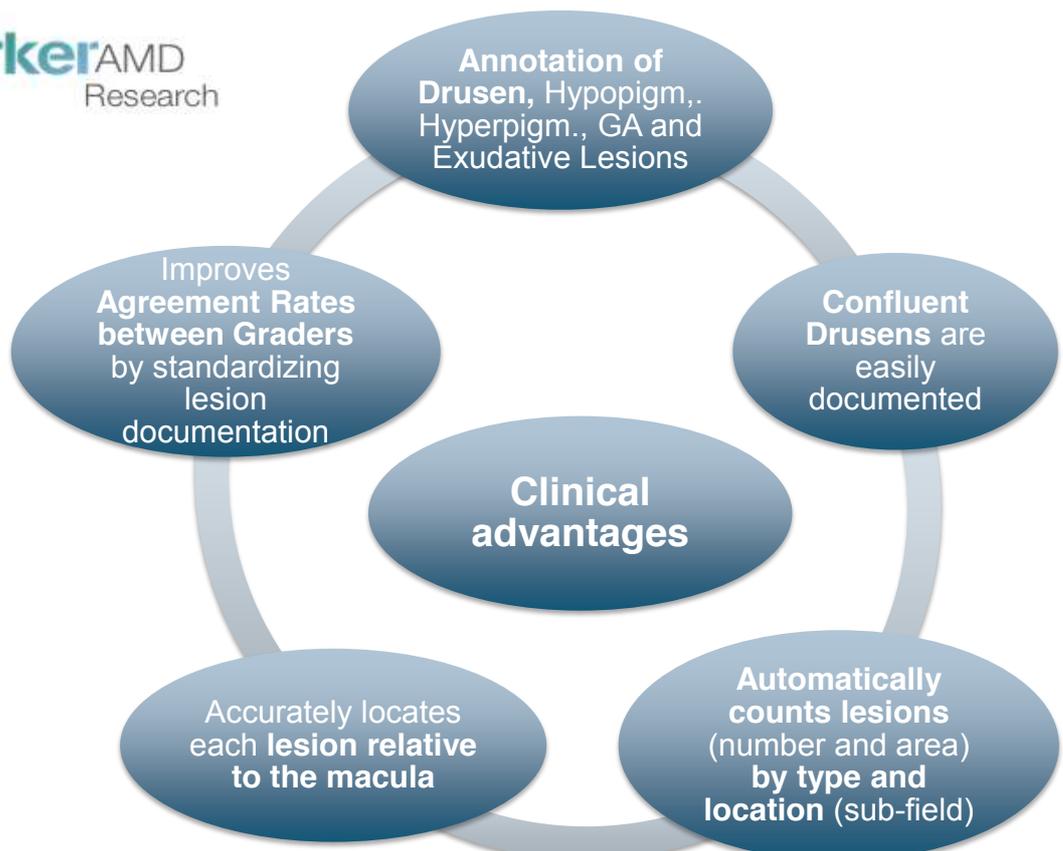
- Microsoft Windows XP with Service Pack 3
- Account with Administrative Rights to run & install the Software

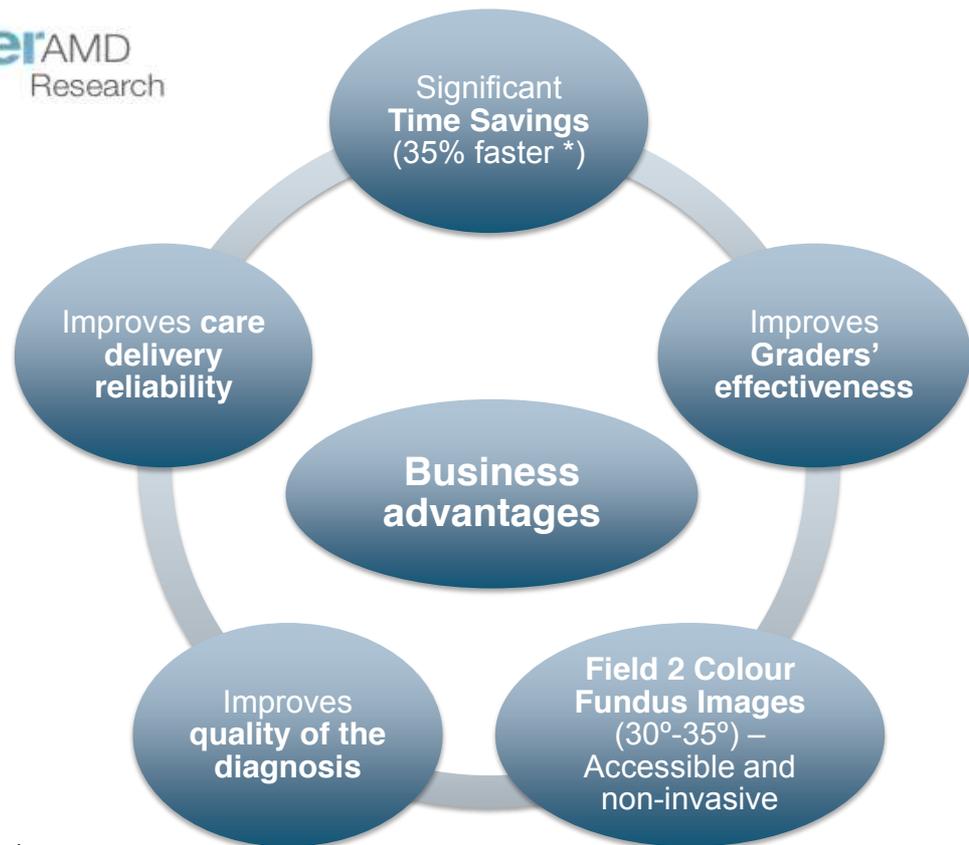
## Retmarker uses/installs the following components

- Microsoft SQL server 2005 compact edition (free)
- Mathworks Matlab Runtime 7.9 (free)
- Microsoft Framework .NET 3.5 (free)
- Microsoft Framework .NET 2.0 (free)



### Computer-assisted AMD grading tool





\* Based on small study comparing manual grading method and RetmarkerAMD.

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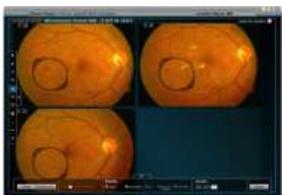
## Thinking ahead

### Undergoing developments

- Retmarker AMD application for Clinical Practice
- DR Screening system

### Current platform

- Image inspection and annotation tools.
- Co-registered image comparison, allowing assessment looking at previous images.
- Patient reports / educational tool.



### Available Algorithms

- Automatic Image Enhancement.
- Co-registration (automatic overlap of different exams).
- Difference detection.
- Microaneurysm turnover (based on MA detection).

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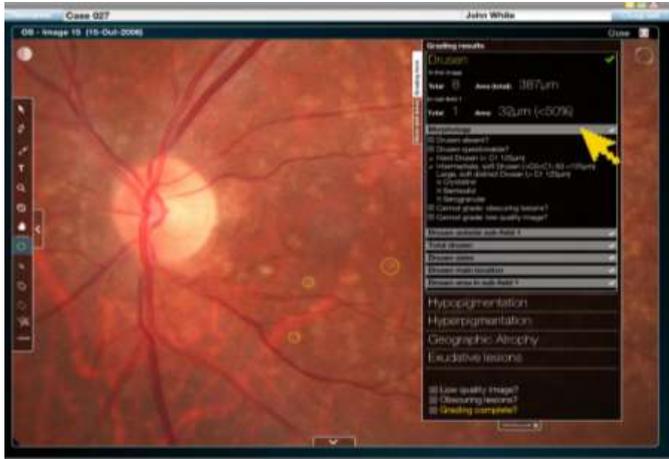
## Biomarker for Age-related Macular Degeneration progression.

Monitoring of Drusen activity.

- number;
- area;
- rate of change.

Highlighting of lesion evolution trends toward the macula.

Correlation of lesion evolution with prescribed treatments.



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### Results:

- Sensitivity: 96%  
**(urgent cases: 100%).**
- Specificity: 52%
- No Disease  
(filtering capacity) = 48%

### Study shows:

- The “Microaneurysm and Vascular lesion detector” (from Retmarker DR) revealed as a safe solution for Disease/No Disease detection in 5.386 patients (21.544 images dataset).

### Further developments:

- Cascade - incorporate other algorithms:
  - Difference Detection
  - Exudate classifier (for later stage DR)

### Potential Applications:

- Patient prioritization;
- Quality assessment;
- Standardizing or second opinion tool to grader;
- Detailed grading tool.





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