Early Detection Tools for Alzheimer's Disease

By

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School of Pharmacy

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Declaration

It is hereby declared that

1. The thesis submitted is our own original work while completing degree at BRAC University.

2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.

3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.

4. We have acknowledged all main sources of help.

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The thesis titled “Early Detection Tools for Alzheimer's Disease” submitted by Ashfaqur Rahman Fahim of Spring, 2025 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy

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Dedication

I dedicate this work to Allah (SWT), whose endless mercy, guidance, and blessings have carried me through every step of this journey. To my beloved parents, whose love, prayers, and sacrifices and unwavering faith in me have been my greatest strength. And to the people I have lost, whose presence I deeply miss, this journey is also for you—a tribute to our little infinity.

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List of Acronyms

MCI – Mild Cognitive Impairment

MRI – Magnetic Resonance Imaging

fMRI – Functional Magnetic Resonance Imaging

PET – Positron Emission Tomography

CSF – Cerebrospinal Fluid

EEG – Electroencephalogram

AI – Artificial Intelligence

ML – Machine Learning

DL – Deep Learning

APOE – Apolipoprotein E

APP – Amyloid Precursor Protein

PSEN1 – Presenilin 1

PSEN2 – Presenilin 2

Aβ – Amyloid Beta

NfL – Neurofilament Light Chain

GFAP – Glial Fibrillary Acidic Protein

p-Tau – Phosphorylated Tau

DTI – Diffusion Tensor Imaging

PiB – Pittsburgh Compound B

OCT – Optical Coherence Tomography

Abstract

Alzheimer's disease (AD) is the most common cause of dementia and affects millions of people around the world. The number of cases is expected to almost triple by 2050 and which makes early detection extremely important. Early detection is critical, as pathological changes such as amyloid-beta plaques, tau tangles, neuroinflammation, and synaptic dysfunction begin decades before clinical symptoms appear. Current diagnostic tools which include neuroimaging techniques like MRI and PET scans, fluid based biomarkers from cerebrospinal fluid and blood, genetic markers such as APOE ε4, and emerging approaches like salivary and retinal biomarkers. AI and machine learning are increasingly being used to analyze imaging, biomarker, and behavioral data, improving accuracy and enabling personalized risk assessments. New technologies such as, wearable sensors and non-invasive molecular diagnostics are showing promise for real-time monitoring and large-scale screening. But still they need more research before becoming reliable. This review evaluates at both traditional and new methods for early detection, discussing their advantages, limitations, and the challenges of making them accessible and standardized. It also highlights the importance of multi modal strategies that combine biomarkers, imaging, and AI to identify AD in its earliest stages. Creating opportunities for timely treatment, clinical trial involvement, and better outcomes for patients.

Keywords: Alzheimer's disease; early detection; biomarkers; neuroimaging; artificial intelligence; wearable technology; diagnosis

Chapter 1

Introduction

1.1 Alzheimer's Disease

Alzheimer's disease (AD) is a devastating neurological condition characterized by the progressive degeneration of brain tissueAs the primary contributor to dementia cases globally, AD accounts for approximately 60-80% of all instances (Jack et al., 2018; Cummings et al., 2021). People with AD struggle with memory loss, confusion, and changes in behavior, which can be significantly deteriorate their quality of life. Presently, over 55 million individuals are affected by dementia, with projections indicating this figure will triple by 2050 due to aging populations (World Health Organization, 2023).

The disease is caused by two main problems in the brain, including sticky clumps of protein called amyloid plaques that build up outside brain cells, and twisted strands of another protein called tau that form tangles inside brain cells. These pathological features disrupt neural communication pathways and ultimately leading to cognitive deficits and widespread cerebral atrophy (Hampel et al., 2021).

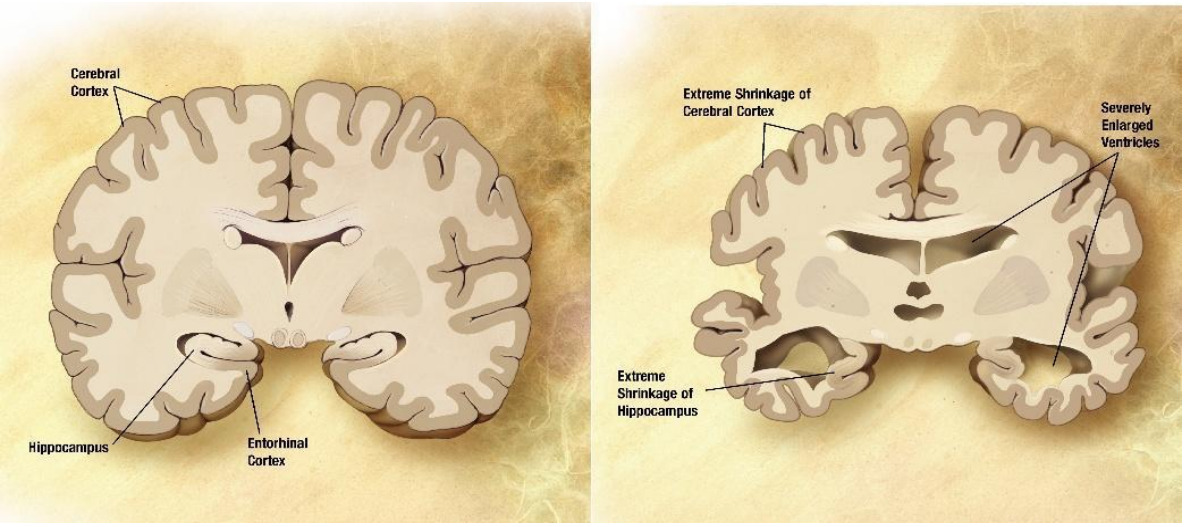

Figure 1: *Comparison of a healthy brain (left) and an Alzheimer's brain (right), showing significant shrinkage and deepened sulci due to neurodegeneration (Wikimedia Commons, 2016)*

In addition to inflammation, problems with energy production in cells, and damage from oxidative stress exacerbate neurodegeneration, speeding up the brain's decline (Heneka et al., 2015).

What's even more alarming is that these destructive processes start long before clinical symptoms appear, sometimes decades earlier (Sperling et al., 2014). This means there's a limited window to diagnose the disease early and potentially intervene before it takes hold.

1.1.1 Historical Background and Discovery

The identification of AD traces back to the early 20th century when Dr. Alois Alzheimer who was a German psychiatrist and neurologist conducted pioneering research that changed the landscape of neurological medicine. In 1906, Alzheimer observed a 51-year-old patient named Auguste Deter exhibiting profound memory deficits, language disturbances, and unpredictable behavior. Following her death, Alzheimer performed an autopsy and identified two major neuropathological hallmarks: abnormal extracellular deposits which is now known as amyloid-beta plaques and intracellular twisted fibers composed of a protein called tau (Hardy & Selkoe, 2002). These pathological features became the defining characteristics of the disease that now bears her name.

For decades, AD diagnosis remained possible only through autopsy, severely restricting opportunities for early clinical intervention. Scientific advancements in molecular biology and neuroimaging during the latter half of the 20th century gradually elucidated the disease's mechanisms. The discovery of genetic risk factors like the APOE e4 allele and the formulation of the amyloid cascade hypothesis further revealed AD's biological complexity. In between 1990s and early 2000s researchers could detect amyloid and tau in the living brain through cerebrospinal fluid tests and neuroimaging. This marked a major turning point, shifting diagnosis from autopsy

to the possibility of identifying the disease earlier to explore cure or treatment strategies. Despite over a hundred years of progress, no cure for AD has been found.

1.1.2 Prevalence and Global Burden

AD currently stands among the most significant public health challenges in the world. It's the most common type of dementia and also currently affects over 55 million people globally. By 2030, the number is expected to rise to around 78 million and by 2050, it could reach around 139 million World Health Organization, 2023; Alzheimer's Disease International, 2022). These growing numbers are driven not just by an increasingly aging population, but also by the fact that there is still no cure—making early diagnosis and intervention more critical than ever.

AD affects far more than those diagnosed; its impact extends to families, caregivers, healthcare systems, and entire economies. In 2018, the global cost of dementia—including medical care, long-term support, and unpaid caregiving—exceeded $1 trillion(Prince et al., 2016; Klyucherev et al., 2022), a figure projected to rise sharply in the coming decades. Many families bear substantial out-of-pocket expenses for home care or residential facilities, while caregivers often face reduced work hours or career interruptions. In low- and middle-income countries, where AD prevalence is expected to grow most rapidly, economic and healthcare systems frequently lack the capacity and resources to manage this escalating burden (World Health Organization, 2023). This multifaceted burden underscores the urgent need for policies that emphasize prevention, early diagnosis, and support systems—both medical and social to mitigate the far-reaching consequences of the disease (Prince et al., 2016; Brookmeyer et al., 2018).

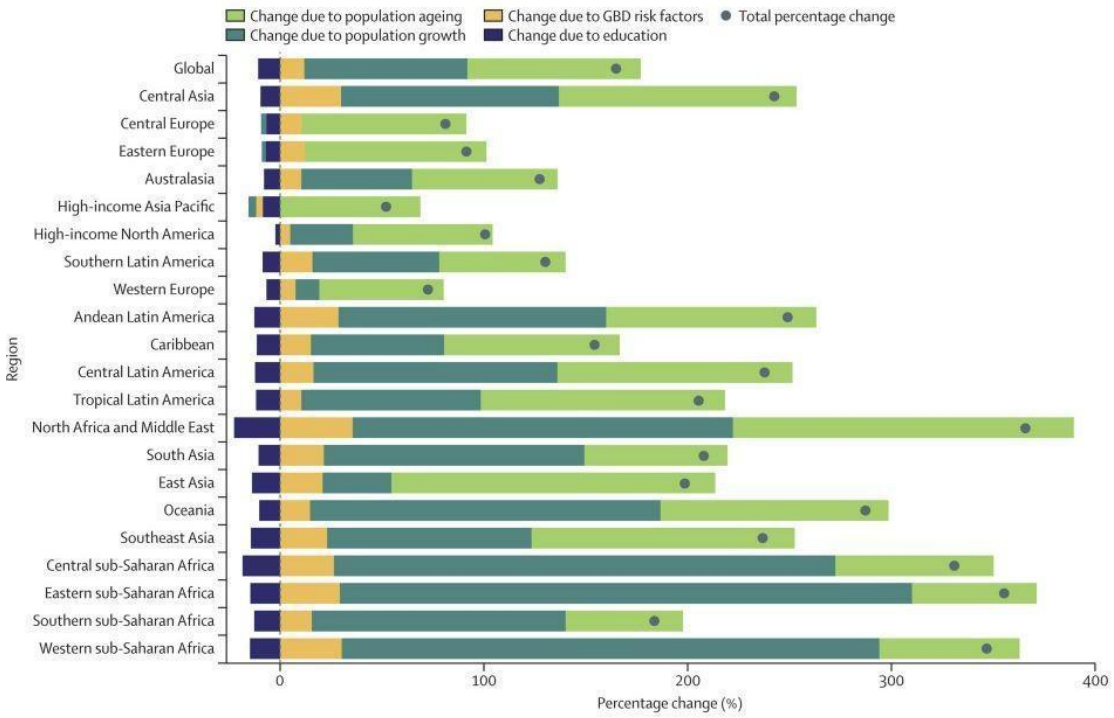

Figure 2: *The statistic about 55 million cases and projected tripling by 2050. (Alzheimer's Clinics, n.d.)*

1.1.3 Clinical Manifestations and Progression

Alzheimer's doesn't happen overnight. It creeps up slowly, usually in three stages. First, there's the "preclinical" stage, where the brain starts to change years before any symptoms appear. This is the best time to intervene but is also the hardest to detect (Bateman et al., 2012).

Next one is mild cognitive impairment (MCI) where people start to notice small memory lapses or trouble thinking clearly. These changes aren't severe enough to disrupt daily life, but they can be a warning sign that Alzheimer's is on the horizon.

Finally, there's the dementia stage, where the disease takes over. People lose their ability to remember anything, making decisions, or even communicate with others. They may become confused, agitated, or withdrawn. Eventually, they'll need round the clock care (Dubois et al., 2014). The damage starts in the hippocampus, the part of the brain that helps form memories. Over

time, it spreads to the cerebral cortex, which controls things like thinking, speaking, and making decisions. As the disease progresses, the brain gets smaller, and the person slowly loses their memories, abilities, and sense of self (Sweeney et al., 2018).

1.2 Pathophysiology of AD

AD is a complex condition that slowly damages the brain. Researchers have found several factors behind this damage, including clumps of amyloid-beta proteins, tangles of tau proteins, and widespread inflammation in the brain. These problems interfere with how brain cells talk to each other, leading to memory loss, confusion, and other symptoms.

1.2.1 Amyloid-Beta Plaques: The Core Problem

At the center of AD is a harmful buildup of a protein fragment called amyloid-beta (Aβ). In a healthy brain, Aβ is cleared away naturally. But in Alzheimer's, this cleanup system stops working. Instead, a larger protein called amyloid precursor protein (APP) gets broken down the wrong way by certain enzymes (like β-secretase and γ-secretase), creating sticky Aβ pieces. These clump together and become toxic to brain cells. These fragments stick together and form plaques (Hardy & Selkoe, 2002). The plaques interfere with communication between brain cells, trigger

inflammation, and damage mitochondria, the part of cells that generate energy (Heneka et al., 2015). Interestingly, it's not just the big plaques that cause trouble, small clusters of Aβ, known as oligomers, seem to do the most damage by interfering with transmission of synapses, the connections critical for memory (Sweeney et al., 2018).

1.2.2 Tau Tangles: When Structure Fails

Another major player in AD is tau, a protein that normally helps stabilize the structure inside neurons. In AD, tau becomes overloaded with phosphate groups, making it malfunctional. Instead of supporting the cell's framework, abnormal tau detaches and forms tangled threads within neurons (Dubois et al., 2014). These tangles initially develop in the memory related regions like the hippocampus, and then spread to other parts of the brain, mirroring the progression of symptoms (Jack et al., 2018). Recent research suggest that if once tau proteins become misfolded, they can spread to neighboring brain cells in a way that resembles an infection and can cause further damage (Blennow et al., 2010). This spread of abnormal tau is believed to play a key role in the progression of AD.

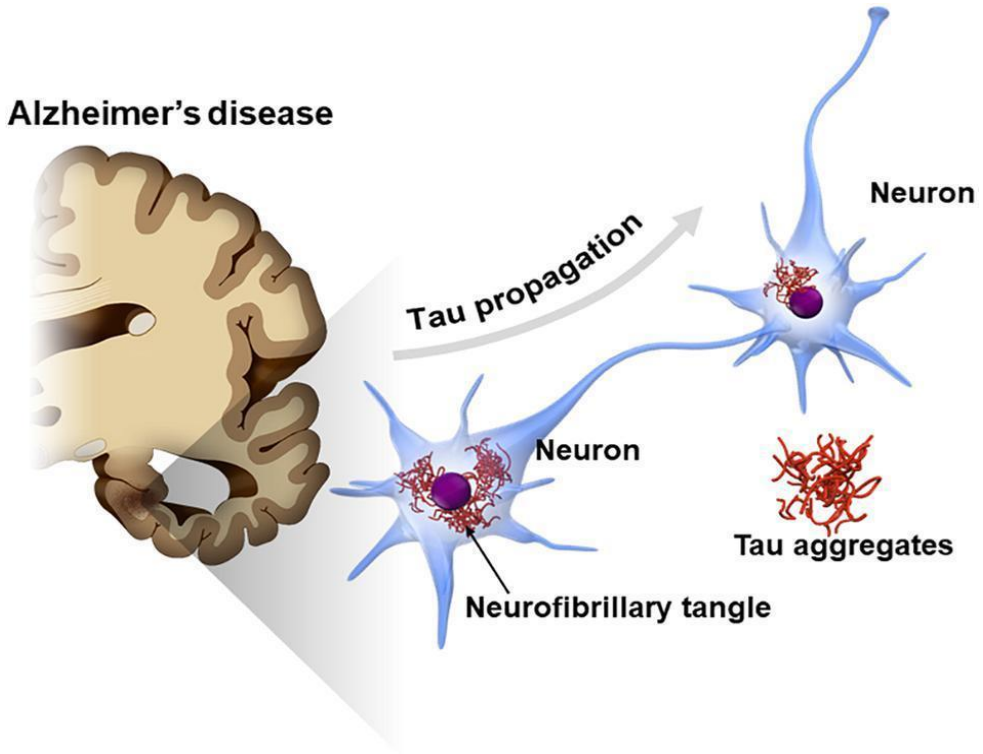

Figure 3: *Propagation of tau pathology in Alzheimer's disease brain. (Frontiers in Neuroscience, 2019)*

1.2.3 Synaptic Dysfunction and Neuronal Death

Even before memory loss becomes noticeable, the connections between brain cells called "synapses", crucial for thinking and memory begin to break down. When Aβ and tau disrupt brain function, early signs of cognitive decline begin to show (Sweeney et al., 2018). And the damage gets worse over time and leading to the death of neurons, especially in key areas like the hippocampus and prefrontal cortex. Which are important for memory and decision making. Several factors contribute to this damage, including oxidative stress, mitochondrial dysfunction, and high calcium levels in brain cells. All of these raise the chances of neuronal death. Brain scans reveal that when these neurons are lost, the affected parts of the brain shrink (Heneka et al., 2015; Guzman-Martinez et al., 2019).

1.2.4 Neuroinflammation

While neuroinflammation starts as a protective response to neuronal death, it often ends up making things worse. A key player in this process that is a type of brain cell called microglia, which works like the brain's cleaning crew and they move in to clear out amyloid plaques, dead cells, and other waste (Heneka et al., 2015). At first, this cleanup response is helpful but if the microglia stay activated for too long, they begin releasing harmful chemicals like cytokines and free radicals. These substances can damage nearby neurons and make the inflammation worse, creating a vicious cycle.

Another important type of brain cell is the astrocyte. In a healthy brain, astrocytes support neurons by regulating blood flow, delivering nutrients, and maintaining balance in the brain's environment. However, in AD, astrocytes often stop functioning well. They become very reactive and may even contribute to the damage (Heneka et al., 2015).

What makes this situation more difficult is that the inflammation doesn't happen on its own. It's connected to other problems in the brain like Aβ and tau pathology. These abnormal proteins can activate microglia as well as astrocytes and starting the inflammation process. On top of that, the factors like genetics, environment, and overall immune health can influence how severe the inflammation becomes. Because of the intricate pathways, researchers are now looking more closely at inflammation as a target for treatment. The emerging anti-inflammatory therapies to slow down the progression of AD can be used as a potential treatment strategy. While more research is needed, there is still a lot to explore that targeting inflammation could be a promising approach for treating AD (Heneka et al., 2015).

1.3 Why Early Detection is Critical for Delaying Progression and Improving Patient Outcomes?

Early detection means starting treatments on time, making lifestyle changes, and planning for the future. Detecting AD during preclinical or prodromal stages offers important chances to intervene before irreversible brain damage happens.

1.3.1 Slowing the Disease with Early Treatment

One of the main benefits of diagnosing AD early is that treatments work better in the initial stages. Medications like donepezil and memantine can help manage symptoms, but they are most effective when brain function is still fairly intact (Blennow et al., 2010). Similarly, newer therapies that target amyloid plaques, such as aducanumab and lecanemab, show better results when started before significant nerve damage occurs (Cummings et al., 2021). Early detection allows for timely intervention, which helps patients keep their productivity and health.

1.3.2 Lifestyle Changes

Early diagnosis of AD lets patients take effective steps to support and protect brain health. Small lifestyle changes, such as eating a healthy diet, exercising regularly, and staying mentally active, can be very helpful. For example, regular physical activity improves blood flow to the brain and reduces inflammation, which may help slow down memory decline (Sweeney et al., 2018). Engaging in activities like reading, solving puzzles, or socializing can also keep the mind sharp. Over time, these habits can have a significant positive impact on cognitive function.

1.3.3 Clinical Trials and Experimental Therapies

Early diagnosis opens the door to clinical trials for new therapies. This gives patients the chance to try treatments that are not yet widely available. Many of these experimental therapies target individuals in the early stages of Alzheimer's disease, when they are likely to work best (Bateman et al., 2012). By participating in a trial, patients might receive access to new therapies while also assisting researchers in discovering better treatments for the future (Dubois et al., 2016).

1.3.4 Reducing Healthcare Costs

Early diagnosis can help delay the need for full-time care, saving money for families and healthcare systems (Brookmeyer et al., 2018). Preventing or slowing AD through early intervention could also reduce the massive global cost of the disease. (World Health Organization, 2023).

1.4 Challenges in Detection of AD

Diagnosing AD early is very difficult for many reasons. This disease is very complex, symptoms vary widely. In addition the current tools for diagnosis have limitations like Cognitive tests, Brain

Scans and Biomarker tests. These challenges make it harder to treat AD early when treatments can be most effective. By understanding these challenges is really important for finding better ways to detect AD early. It also can help to make sure that more people get the right diagnosis and the support they need at the right time.

1.4.1 Different Symptoms

Patients experience variable symptoms such as memory loss, trouble with speaking, solving problems, or even recognizing faces and finding their way. (Dubois et al., 2014; Jack et al., 2018). Because of these differences AD is sometimes confused with other types of dementia, like Lewy body or vascular dementia. In some cases, memory problems might even be mistaken for conditions like anxiety or depression (Ard et al., 2021).

1.4.2 Limitations of Current Tests

Doctors usually diagnose AD by using a mix of memory tests, brain scans, and tests for biological markers. But each of these has some limitations:

· **Cognitive Tests:** In cognitive tests, the tools like Mini Mental State Exam (MMSE) and the Montreal Cognitive Assessment (MoCA) are commonly used. Because they are really quick and easy to administer. But they're not always perfect. Because they often miss the subtle signs that show up in the early stages of AD (Prince et al., 2016).

· **Brain Scans:** Imaging tools such as MRI and PET scans can show some changes in the brain that are linked to AD, such as, shrinking in certain areas or a buildup of amyloid plaques (Jack et al., 2018). But these scans are very expensive and may be unavailable, especially in rural areas or small clinical settings (Jack et al., 2018; Brookmeyer et al., 2018).

· **Biomarkers:** Biomarker tests look for certain proteins like Aβ and tau in spinal fluid to help diagnose AD. These proteins can indicate changes in the brain associated with the disease. However, the process requires a lumbar puncture, which is invasive and uncomfortable (Blennow et al., 2010). Researchers are trying to develop blood tests for these same markers. This would offer a less invasive option, but these tests are still in the early stages of development and need more validation to ensure their accuracy (Zhang et al., 2022).

1.4.3 Cost and Accessibility Issues

Getting tests for AD, like PET scans or biomarker testing, is not always easy or affordable. These tests can be very expensive. For many people, especially those living in low-income or rural areas, they can be hard to access (Sweeney et al., 2018). In some parts of the world, healthcare systems don't have the money, resources, or trained professionals to offer these tests (World Health Organization, 2023). As a result, many people, such as older adults and those from underserved communities, face delays in getting diagnosed.

1.4.4 Ethical Concerns with New Technology

New tools like AI and wearable devices are creating exciting ways to detect AD in its early stages. For example, AI can analyze brain scans to identify early changes. Smart devices can monitor a person's cognitive performance over time.

However, despite the promise of these innovations, they raise serious concerns. This is especially true regarding privacy, data accuracy, and whether the technology is fair for everyone (Heneka et al., 2015; Zhang et al., 2022).

1.5 Objectives of the Study

The main goal of this review is to provide a critical assessment of the tools currently available for the early detection of AD and to identify opportunities for their enhancement. It also suggests practical strategies to connect research findings with clinical use. Specific objectives have been outlined based on the challenges and opportunities mentioned earlier. The focus is on improving the accuracy, accessibility, and fairness of AD diagnosis while encouraging innovation and progress in early detection methods.

1.5.1 Reviewing Existing Early Detection Tools

The first goal of this review is to examine the tools used to detect Alzheimer's disease in its early stages. This includes traditional methods like memory and thinking tests, brain scans such as MRI and PET, and spinal fluid tests that check for specific proteins. We can also explore newer methods like blood tests, digital health tools, and technologies that use AI to assist with diagnosis (Jack et al., 2018; Zhang et al., 2022). The aim is to understand how well each method works in real medical settings by examining both their strengths and weaknesses.

1.5.2 Identifying Gaps in Our Understanding

Researchers have made considerable progress in developing early detection tools for AD. However, many important questions remain unanswered. One major challenge is identifying biomarkers that are sensitive and accurate enough to distinguish AD from other types of dementia (Blennow et al., 2010). Genetic factors, lifestyle, and environmental influences can affect early detection (Heneka et al., 2015). By highlighting these gaps in our knowledge, this review aims to guide future research to areas that need the most focus.

1.5.3 Exploring New Technologies

The fast advancements in technology are changing how we detect AD. Tools like AI, machine learning, and wearable devices show real promise for early detection methods. These methods are not only accurate and non-invasive, but they are also more affordable and convenient (Zhang et al., 2022; Sweeney et al., 2018). For example, AI can analyze large volumes of data, such as brain scans, electronic medical records, and genetic profiles, to identify early warning signs of the disease that doctors might overlook. Additionally, wearable devices can monitor changes in thinking and behavior over time, providing doctors with valuable information to take timely action.

Chapter 2

Methodology

To complete this review project, I went through a wide range of published journal articles and gathered relevant information from renowned scientific sources such as PubMed, Google Scholar, SpringerLink, and Science Direct. To get information, I applied specific keywords including "Alzheimer's disease," "early detection tools," "biomarkers," "neuroimaging," "cognitive assessment," and "genetic risk factors." These keywords helped me to narrow down the articles that specifically discussed detection methods for Alzheimer's disease rather than focusing on treatment or unrelated neurological conditions.

From this process, I selected research papers, systematic reviews, clinical trial reports, and meta-analyses published mainly between 2010 and 2024. I excluded articles that did not directly discuss diagnostic or detection strategies. This includes those that focused exclusively on treatment interventions or unrelated neurological disorders. This approach kept the review focused on methods relevant to identifying Alzheimer's disease in its earliest stages.

Information gathered from the selected sources was organized into categories, including traditional diagnostic approaches, biomarker-based tools, imaging techniques, artificial intelligence applications, and new non-invasive technologies. In each category, I assessed both the strengths and weaknesses of the tools along with their potential for use in clinical practice.

Figures and diagrams included in this review were collected from previously published sources to support explanations of concepts and processes. Each figure is properly referenced to its original publication, ensuring both clarity and academic integrity.

Regarding my literature review process, I collected information manually from each chosen article. I read and summarized the findings, then put them together into a clear narrative. Instead of using automated tools, I organized the information by grouping the detection methods into categories

like imaging techniques, fluid biomarkers, neuropsychological tests, and computational approaches. All references used in this project have been cited correctly to uphold academic integrity.

Chapter 3

Results

3. Results

A quick overview table highlighting each tool, how it works, advantages, and its limitations:

Tool Category	Examples	Advantages	Limitations	References
Neuroimaging	MRI, PET scans (Amyloid imaging),	High spatial resolution for detecting structural/pathological changes	Costly, limited accessibility	Blennow et al., 2010; Villemagne et al., 2013
Biomarkers	CSF Aβ42, Tau, Plasma Aβ, NfL, GFAP	High specificity for AD pathology (CSF); less invasive (blood/plasma)	Invasive (CSF), variability in blood tests	Bateman et al. (2012); Blennow & Zetterberg (2018); Klyucherev et al. (2022); Kim et al. (2023)
AI-Based Tools	ML algorithms	Scalability, pattern recognition	Scalability, efficient pattern recognition in complex datasets	Zhang et al. (2022); Kale et al. (2024); Laske et al. (2015)
Emerging Technologies	Wearable sensors	Non-invasive, real-time monitoring	Early validation stage	Ausó et al., 2020; Ogbodo et al., 2022; Kulichikhin et al., 2021

Chapter 4

Discussion

4.1 Neuroimaging Techniques

Neuroimaging is vital for the early detection AD. It helps clinicians and researchers see physical and chemical changes in the brain before symptoms appear. These non-invasive scans allow a detailed examination of brain structure and function. They reveal features like brain atrophy, the buildup of amyloid-beta (Aβ) plaques, the formation of tau tangles, and changes in connectivity and communication between different brain regions. The main types of brain scans used for AD are structural MRI, PET scans, functional MRI (fMRI), and Diffusion Tensor Imaging (DTI). Each scan has its own strengths and weaknesses, but together they provide valuable information for diagnosing the disease and studying its progression. (Blennow et al., 2010; Dubois et al., 2014; Villemagne et al., 2013).

4.1.1 Role of MRI in Detecting Early Brain Atrophy

Structural MRI is one of the most useful tools for identifying early neurodegenerative changes. It helps spot shrinkage in specific parts of the brain, particularly the hippocampus and the medial temporal lobe. These areas are crucial for memory and are often affected early in the disease (Dubois et al., 2014; Jack et al., 2018). The shrinkage of the hippocampus seen in MRI scans consistently links to progression from mild cognitive impairment (MCI) to Alzheimer's disease (AD). It also serves as a reliable anatomical marker for disease progression (Sweeney et al., 2018). These brain changes appear before significant memory loss occurs, meaning MRI can help identify people at risk before their condition worsens.

4.1.2 Use of Positron Emission Tomography (PET) for Aβ and Tau Protein Imaging

PET scans are very useful for detecting specific brain changes related to AD. One type, called amyloid PET, uses special tracers like Pittsburgh Compound B (PiB) to identify where Aβ plaques accumulate in the brain. This helps doctors distinguish AD from other brain disorders (Villemagne et al., 2013). Another type, tau PET, uses tracers like flortaucipir (AV-1451) to indicate where tau tangles are forming. These tangles are closely related to the progression of the disease and the decline in a person's thinking ability (Bateman et al., 2012). These scans provide researchers and doctors with a clearer view of what is happening inside the brain. They are especially helpful in selecting the right patients for clinical trials.

4.1.3 Advancements in Functional MRI (fMRI) and Diffusion Tensor Imaging (DTI) for Tracking Brain Connectivity Changes

fMRI and DTI are brain scanning methods that examine functional and microstructural brain integrity. They do more than just show what the brain looks like. They help us understand how well it is working and how its internal wiring is holding up. For example, fMRI can detect problems in areas like the default mode network (DMN), which is involved in memory and often shows early signs of trouble in Alzheimer's disease (Blennow et al., 2010). DTI, on the other hand, focuses on the brain's white matter, the “highways” that connect different parts of the brain. It can identify small changes in these pathways even before the brain starts to shrink (Sweeney et al., 2018). These techniques simplify early detection by capturing shifts in brain connectivity and add more layers to diagnostics. However, these tools are powerful, and they come with significant challenges. MRIs and PET scans are very expensive and require trained experts. This makes them hard to use in areas with limited resources (Brookmeyer et al., 2018; Jack et al., 2018). PET scans

also require the use of radioactive substances, and therefore are not ideal for regular checkups in large groups of people. So even though brain scans are great for studying how Alzheimer's develops and spotting early problems, they're not yet practical for large scale screening.

Researchers are working hard to make these technologies cheaper, easier to use, and more common in everyday healthcare sectors. Combined with other tools like blood tests and AI, brain scans can becoming more useful and accessible and these improvements could help us find AD earlier, easily and more effectively, even in larger populations (Zhang et al., 2022; Laske et al., 2015).

4.2 Biomarkers

Biomarkers have become essential tools for early detection and diagnosis of Alzheimer's disease. They help doctors and researchers identify changes in the brain that might occur years or even decades before memory or thinking issues arise. These biological markers show what might be going wrong in the brain, including the buildup of amyloid-β (Aβ) plaques, abnormal tau protein formation, brain cell damage, and inflammation. In recent years, the use of biomarkers has grown in both medical practice and research. For example, the National Institute on Aging and the Alzheimer's Association (NIA-AA) have created guidelines that define Alzheimer's disease based on these biological signs instead of only focusing on clinical symptoms (Jack et al., 2018). Common biomarkers come from several sources: cerebrospinal fluid (CSF), blood samples, genetic testing, and new methods like saliva analysis and retinal imaging. Each method has its own benefits and drawbacks. Some provide greater accuracy. Others are less invasive, while some may be more affordable or simpler to carry out.

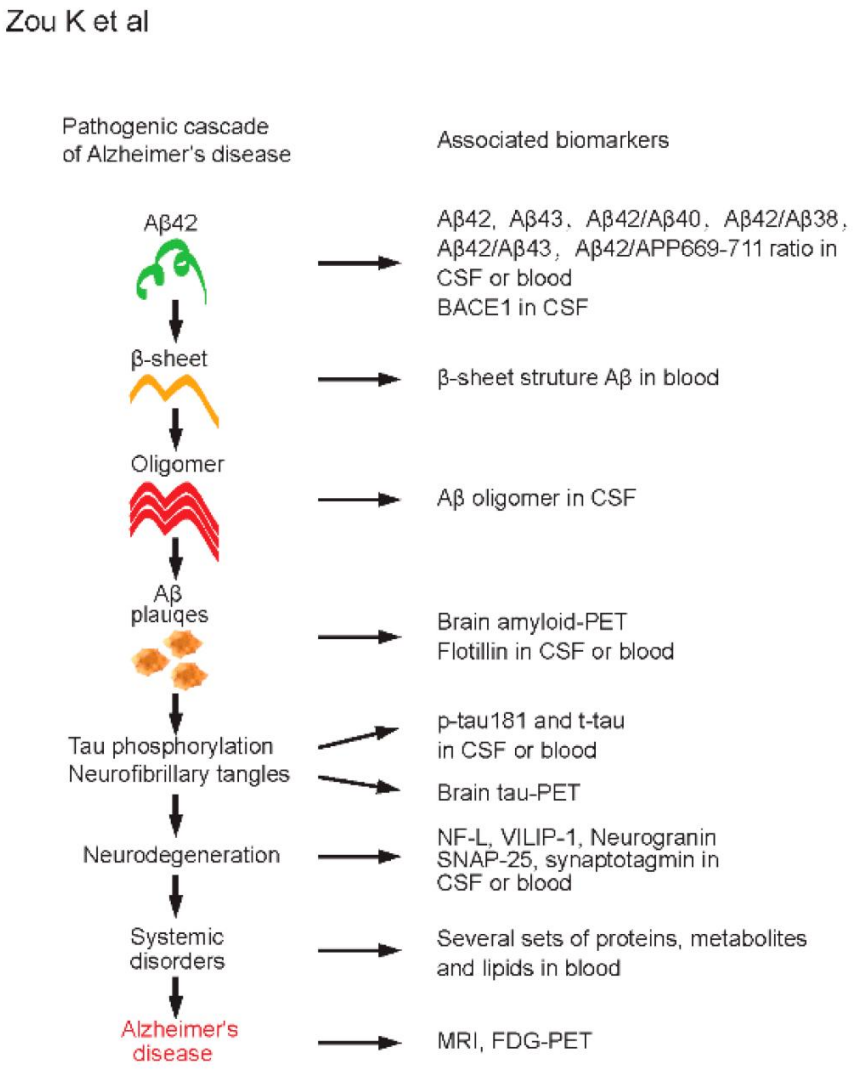

Figure 4: Alamy. Alzheimer's disease: amyloid plaques, neurofibrillary tangles illustration

4.2.1 Cerebrospinal Fluid (CSF) Biomarkers

CSF biomarkers are currently some of the most reliable and well-researched tools for detecting AD in its early stages. They provide doctors with a close look at what's happening in the brain on a molecular level, even before any symptoms appear. The three main CSF biomarkers commonly used are amyloid-beta 42 (Aβ42), total tau (t-Tau), and phosphorylated tau (p-Tau). These three biomarkers create a signature profile that has been strongly linked to the progression of the disease, including its preclinical and prodromal stages. In people with AD, the amount of Aβ42 in the CSF

usually decreases because it starts clumping together and forming plaques in the brain. This drop in Aβ42 clearly indicates plaque buildup (Bateman et al., 2012). At the same time, levels of t-Tau and p-Tau increase. High t-Tau levels suggest that brain cells are getting damaged, while high p-Tau levels indicate the formation of tangles inside the brain cells; both are classic signs of AD (Blennow et al., 2010; Blennow & Zetterberg, 2018). When all three biomarkers are measured together, they create a pattern that is strongly connected to AD, even in the very early stages before dementia begins.These CSF markers are not only useful for diagnosing AD but can also help doctors determine how far the disease has progressed and how likely it is to worsen. Studies have shown that these biomarkers can accurately predict when someone with mild cognitive issues is likely to develop AD dementia (Bateman et al., 2012). Because of their reliability, these biomarkers have been included in official diagnostic guidelines like the NIA-AA research criteria (Jack et al., 2018). In fact, having low Aβ42 along with high t-Tau and p-Tau is now seen as a clear biological signal of AD (Dubois et al., 2014).

Still, there are some drawbacks. To get CSF, doctors need to perform a lumbar puncture that is also called a spinal tap, which is invasive and can make patients uncomfortable or nervous. Because of this, CSF tests aren't always practical for regular use in everyday doctor visits, especially in family clinics (Blennow & Zetterberg, 2018). But in specialized centers and research areas, CSF testing is still considered a gold standard because of its accuracy and sensitivity for early detection of AD.

Overall, CSF biomarkers are incredibly useful for understanding what's going on in the brain with AD as they allow for very earlier and more accurate diagnoses based on biology, rather than just symptoms. In addition to the brain imaging, blood tests, and newer digital tools, CSF biomarkers

help create a more complete picture of a persons risk for AD and how the disease is progressing (Blennow et al., 2010; Jack et al., 2018; Dubois et al., 2014).

4.2.2 Blood-Based Biomarkers

Blood based biomarkers have emerged as promising invasive alternatives to CSF analysis for early AD detection and monitoring. Because they offer a much easier and less invasive way to detect and track the disease compared to spinal fluid tests. As these biomarkers are derived from blood plasma, they offer the advantage of being more accessible, less invasive, and more scalable for population level screening especially when compared to the lumbar puncture needed for CSF collection even though they're still being fully tested and verified (Blennow & Zetterberg, 2018; Sweeney et al., 2018). These blood tests are showing a lot of positive results in identifying key Alzheimer's processes like amyloid buildup, brain cell damage, and inflammation.

One of the most researched blood-based biomarkers is the ratio of Aβ42 to Aβ40 in the blood.. This ratio closely matches the amount of amyloid plaque in the brain, as confirmed by PET scans. When the ratio drops, that means amyloid plaques are forming just like when Aβ42 drops in CSF (Sweeney et al., 2018). This is an important breakthrough because it means that a simple blood test might eventually replace more complex and expensive procedures. Another marker getting more positive feedbacks is neurofilament light chain (NfL), which shows up when the axons of long fibers that help nerve cells communicate and get damaged. High levels of NfL in the blood have been linked to worsening disease. Although it is not unique to AD, but it is still a solid marker of overall brain degeneration (Blennow & Zetterberg, 2018; Villemagne et al., 2013).

Researchers are also studying on glial fibrillary acidic protein (GFAP), which is another plasma biomarker that is under investigation. It reflects inflammation and activity in brain support cells

called astrocytes. Recent studies show that GFAP levels are higher in people with AD especially in the early stages, suggesting it could be useful for spotting the disease early on (Kim et al., 2023).

Still blood based biomarkers have a few barriers to clear before they can be used widely in clinics. A big challenge is variability that differences in lab techniques, patient populations, and stages of disease that can make it hard to get consistent results (Guzman-Martinez et al., 2019). Also, in markers like NfL and Aβ42/Aβ40 provide useful insights and they're not yet specific enough to clearly separate AD from other brain diseases, which can lead to confusion during diagnosis (Klyucherev et al., 2022).

Ongoing research aims to standardize measurement protocols and validate blood markers in large, diverse cohorts. As these efforts mature, blood biomarkers could serve as the foundation for routine screening and early intervention programs, especially when combined with digital tools and artificial intelligence for integrated risk assessment (Sweeney et al., 2018; Blennow & Zetterberg, 2018).

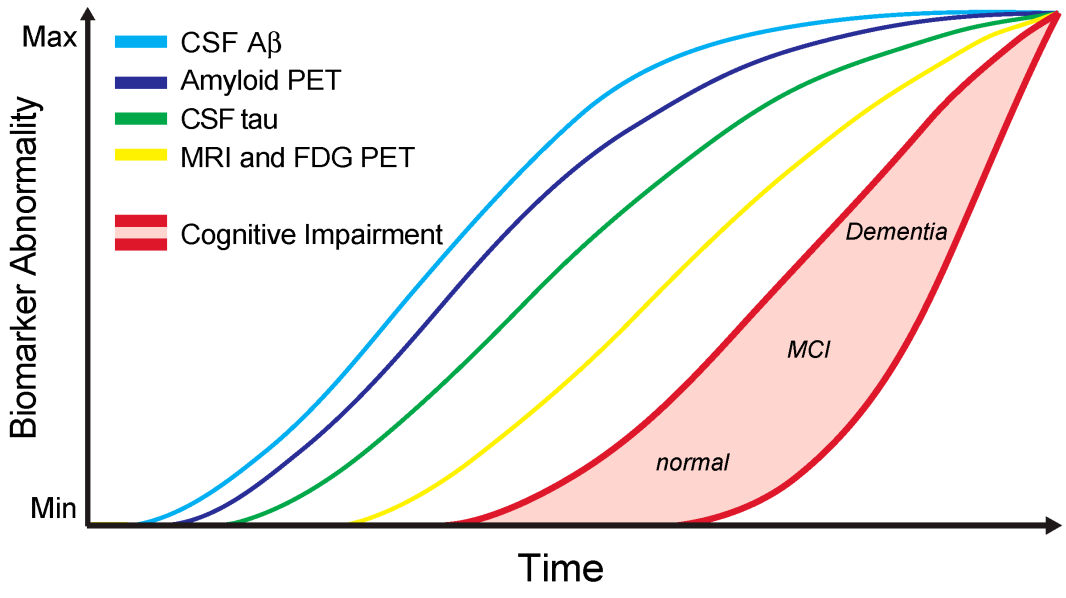

Figure 5: Case examples of MRI/PET heatmaps highlighting regions predictive of MCI-to-AD progression

4.2.3 Genetic Markers

Genetic markers play a critical role in understanding individual susceptibility to AD, especially in distinguishing between sporadic and familial forms of the condition. While genetic testing is not typically used as a standalone diagnostic tool, it provides valuable insights into risk stratification, early identification of at-risk individuals, and guidance for targeted monitoring and intervention strategies.

One of the most well known genetic risk for developing AD after in life is a gene called apolipoprotein E (APOE), especially the ε4 version (or allele). Having this gene variant particularly in APOE ε4 increases the chances of getting AD and often leads to an earlier onset of the disease (Dubois et al., 2016). People who carry one copy of APOE ε4 are already at a higher risk and those who with two copies are at even greater risk compared to those who don't have it at all (Blennow, de Leon, & Zetterberg, 2010). This gene seems to affect on how the brain handles Aβ, a sticky protein linked to Alzheimer's, by making it harder to clear and easier to build up into harmful plaques (Dubois et al., 2014). Still, having APOE ε4 doesn't guarantee the development of AD although it is a major risk factor. On the other hand, there is a more rare and aggressive form of the disease called early onset familial Alzheimer's disease (EOFAD). This type of disease are usually heritable and makes up only a small percentage of all Alzheimer's cases. EOFAD is actually linked to inherited mutations in three specific genes like APP, PSEN1, and PSEN2 (Bateman et al., 2012). These gene mutations cause the body to produce too much or wrongly processed amyloid-beta, leading to faster and earlier buildup of plaques in the brain. People with these mutations can start showing Alzheimer's symptoms in their 30s or 40s. That's why genetic

testing is often recommended for family members who may be at risk so that hey can keep an eye on their brain health and plan for the future (Dubois et al., 2016).

Genetic testing can provide valuable insights into a person's lifetime risk of Alzheimer's, but on its own, it is not enough to diagnose the disease or determine its stage. This is because carrying a gene associated with Alzheimer's does not necessarily mean the person has the condition. Genetic results are most informative when combined with other diagnostic tools, such as spinal fluid or blood biomarkers and brain imaging, which together offer a more comprehensive and accurate assessment (Dubois et al., 2014).

It is equally important to consider the emotional and ethical implications of genetic testing, particularly for individuals who have not yet developed symptoms. Learning about an increased genetic risk can influence mental health, insurance coverage, and long-term life decisions. These potential consequences should be thoughtfully discussed before testing is undertaken.

Overall, genetic markers serve as a crucial piece in the AD diagnostic puzzle. APOE ε4 remains a key predictor of sporadic AD risk, while APP, PSEN1, and PSEN2 mutations are definitive indicators of familial AD. As precision medicine advances, incorporating genetic information into personalized diagnostic and therapeutic strategies will become increasingly important for improving patient outcomes.

4.2.4 Emerging use of saliva and retinal biomarkers

As the demand for non-invasive and scalable diagnostic tools for AD grows, emerging biomarkers in saliva and the retina have gained considerable interest. These novel approaches aim to overcome the limitations of current invasive or high-cost methods like cerebrospinal fluid (CSF) sampling and positron emission tomography (PET) scans. Though still in the early stages of development and clinical validation, salivary and retinal biomarkers offer promising avenues for early screening and large-scale population health monitoring.

- **Salivary Biomarkers**: Represent an attractive option due to the simplicity and non-invasive nature of saliva collection. Preliminary studies have explored the presence of key AD-related proteins, such as tau and amyloid-beta, in saliva. These findings suggest that measurable changes in salivary tau and Aβ concentrations may reflect underlying neurodegenerative processes (Ausó, Gómez-Vicente, & Esquiva, 2020). Because saliva collection is low-cost, painless, and suitable for repeated sampling, it holds significant potential for community-based or at-home screening initiatives. However, the composition of saliva can be influenced by numerous physiological and environmental factors, and current research lacks standardized protocols for reliable measurement and interpretation. These issues must be addressed before salivary biomarkers can be adopted in clinical settings.

- **Retinal Biomarkers**: Offer another promising direction for non-invasive AD detection. The retina, being an extension of the central nervous system, shares structural and functional characteristics with the brain. AD-related changes, including amyloid deposits, vascular abnormalities, and retinal thinning, have been identified in the eyes of affected

individuals (Klyucherev et al., 2022). Technologies such as optical coherence tomography (OCT) and retinal amyloid imaging enable detailed visualization of these changes, providing a potential surrogate for cerebral pathology. Because retinal imaging is already widely used in routine ophthalmic care, it could be repurposed for neurological screening, bringing AD diagnostics closer to widespread clinical implementation.

Despite the encouraging potential of these methods, both salivary and retinal biomarkers are still considered investigational. Further longitudinal studies are necessary to validate their predictive value, reproducibility, and specificity to AD, as opposed to other neurodegenerative or systemic conditions (Klyucherev et al., 2022; Ausó et al., 2020). Also, there are still some technical issues that need to be worked out. Like the differences in the machines used for imaging, how samples are handled, and how the results are interpreted. Before these methods can be used as a regular part of diagnosing AD.

4.3 Artificial Intelligence and Machine Learning in Early Diagnosis

Both AI and ML are continuously changing the way we detect AD before. These tools can analyze a large, complex sets of data and also spot very subtle patterns that are linked to the disease. It also help the doctors to make better decisions. Because AI tools can work on a large scale and pick up on patterns that traditional methods might miss, they hold a lot of promise for improving diagnosis. But they still face challenges—like needing large, high-quality data sets and making sure they’re properly integrated into everyday clinical use.

4.3.1 AI-Driven Image Processing

AI-powered image processing has greatly improved our ability to understand and interpret brain scans like MRI and PET images. This is especially true for spotting early signs of Alzheimer's disease (AD). With the help of smart algorithms, these systems can detect small changes, such as brain shrinkage in areas like the hippocampus and entorhinal cortex. These changes may be too subtle for the human eye to notice (Zhang et al., 2022). For instance, machine learning models trained to analyze amyloid PET scans can identify amyloid-beta buildup, a key feature of Alzheimer's, more accurately than traditional manual methods (Villemagne et al., 2013). Research also shows that AI can combine data from different types of brain imaging, such as fMRI and DTI. This helps uncover early disruptions in how different brain areas communicate, often before memory problems begin (Dubois et al., 2014). Laske et al. (2015) note that these AI tools are more effective than older methods at detecting subtle, hidden changes in the brain. They could be used to screen large groups of people more efficiently. However, the accuracy of these tools still relies heavily on the quality and quantity of brain scan data available, which can vary depending on where the scans are performed (Kale et al., 2024).

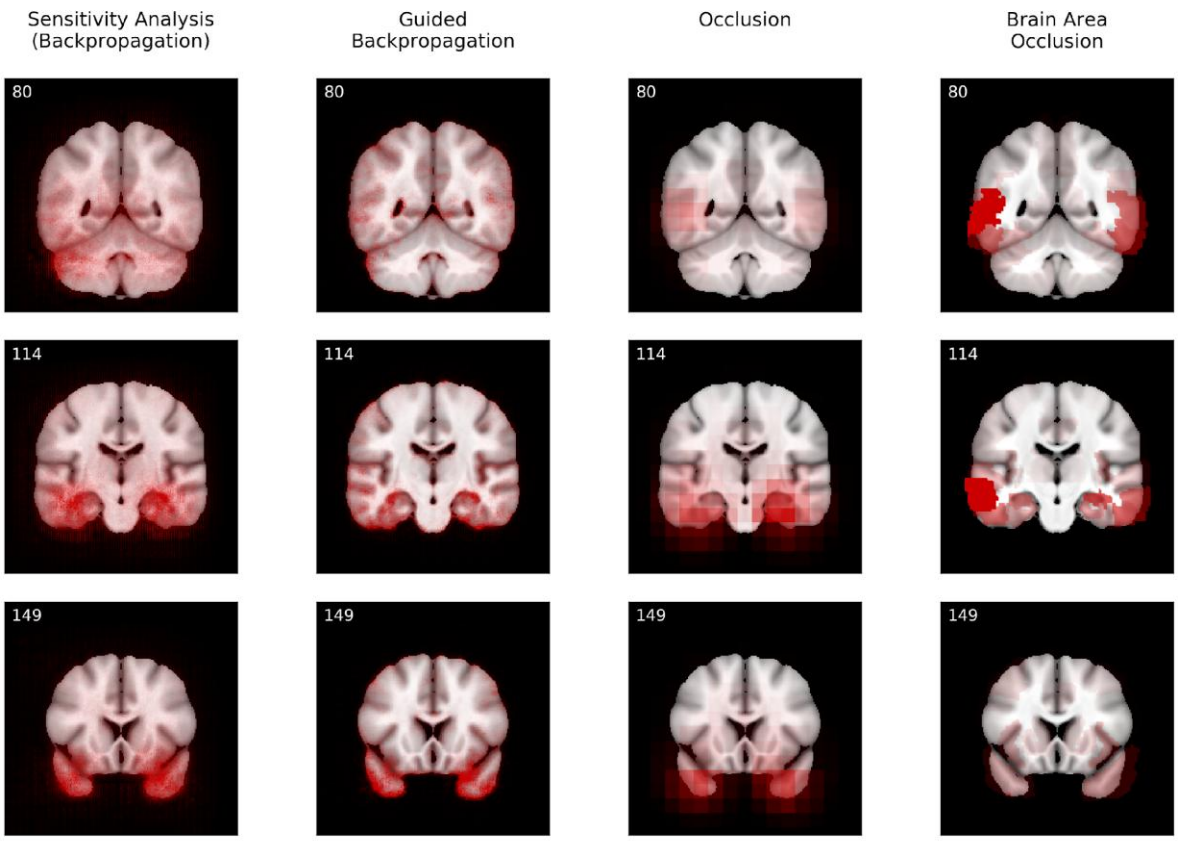

Figure 6: Grad-CAM activation heatmaps overlaid on MRI/PET scans, pinpointing temporal lobe regions crucial for Alzheimer's prediction

4.3.2 Machine Learning Models for Analyzing Biomarker Data

ML models are particularly effective at examining data from biomarkers in both spinal fluid (CSF) and blood to help identify signs of AD. For instance, ML can find important patterns in CSF markers such as Aβ42, total tau, and phosphorylated tau, which are closely tied to the progression of the disease. This leads to more precise results than just relying on standard values (Blennow & Zetterberg, 2018).

Regarding blood-based biomarkers like plasma amyloid beta and neurofilament light chain, which are easier to collect but often less reliable, ML assists by filtering out background noise and combining multiple markers to enhance overall accuracy (Sweeney et al., 2018). Kale et al. (2024)

even showed that ML can merge genetic risk factors, like the APOE ε4 gene, with biochemical data to catch early signs of Alzheimer's that would be nearly impossible to detect by hand. However, for these models to work well, they need to be trained on large and high quality datasets. Also, the differences in how biomarker tests are done across different labs and settings can still create challenges for consistency (Guzman-Martinez et al., 2019). Nevertheless, their ability to process high-dimensional data positions them as a powerful adjunct to traditional diagnostics.

4.3.3 Predictive Algorithms for Risk Assessment and Disease Progression

AI-powered predictive models forecast AD onset and progression. Time-to-event analyses (e.g., Cox proportional hazards models) integrate imaging, biomarker, and demographic data to estimate individualized risk trajectories (Kale et al., 2024). For example, algorithms using amyloid PET and cognitive scores predict conversion from mild cognitive impairment (MCI) to AD dementia with >80% accuracy (Villemagne et al., 2013). Reinforcement learning frameworks also optimize therapeutic trial designs by identifying high-risk cohorts for enrollment (Cummings et al., 2021). However, these models require validation in diverse populations to address racial and ethnic disparities in AD diagnostics (Ard et al., 2021).

4.3.4 Integration of AI with Clinical Practices

AI tools are increasingly embedded into clinical workflows to augment diagnostic accuracy. For instance:

- **Decision support systems:** AI-generated risk scores guide clinicians in prioritizing high-risk patients for invasive tests like lumbar punctures (Laske et al., 2015).
- **Automated reporting:** Natural language processing (NLP) algorithms extract AD-relevant data from clinical notes, reducing human error (Kale et al., 2024).

- **Real-time monitoring:** Wearable sensors paired with AI analyze gait, sleep, and speech patterns to detect functional decline, bridging gaps between clinical visits (Laske et al., 2015).

4.4 Emerging Technologies

Emerging technologies in AD detection increasingly focus on providing accessible, non-invasive, and scalable solutions to identify early changes in the brain before clinical symptoms appear. These innovations build upon existing methods by integrating new scientific approaches, such as biosensing, biofluid testing, and molecular diagnostics. One exciting development is wearable devices that track a person's physical and mental health in real time. These gadgets monitor factors like sleep patterns, walking habits, heart rate changes, and even speech, which can all be linked to early signs of AD (Laske et al., 2015). For example, machine learning algorithms embedded in these devices can detect subtle changes in motor functions, potentially identifying cognitive impairment before it is clinically obvious.

In addition to wearables, researchers are exploring saliva tests as a simple, non-invasive way to screen for AD. Early studies indicate that tau and amyloid-beta, two major proteins involved in the disease, might be found in saliva. This option could be more convenient than testing spinal fluid or blood (Ausó, Gómez-Vicente, & Esquiva, 2020). Although this method is still under investigation, it shows promise as it is inexpensive, easy to collect, and suitable for widespread use in communities.

Retinal imaging has also become a powerful tool. The retina is part of the central nervous system, and changes in the eye, such as amyloid buildup, small blood vessel damage, or thinning of the retina, can reflect what is happening in the brain (Klyucherev et al., 2022). New technologies like

optical coherence tomography (OCT) and fluorescence imaging now allow us to see these changes. Potentially allowing doctors to spot AD during a routine eye check.

Another area showing progress is molecular diagnostics, especially techniques like single cell profiling. These allow scientists to study small changes in individual cells that are linked to early buildup of harmful proteins like amyloid (Kulichikhin et al., 2021). Though it is still in the early testing phase, these tools could help reveal early disease processes and point to new treatment options.

Of course, there are still some challenges. Many of these technologies do not yet have enough long term data. They may face strict regulatory requirements, and need standardized testing procedures. But with continued progress and especially when combined with AI and biomarker tool these innovations could make early AD detection more personalized, affordable, and widely available (Cummings et al., 2019; Zhang et al., 2022).

Chapter 5

Trends and Evolution of Detection Tools Over Time

Trends and Evolution of Detection

The way we detect AD, it has come a long way. It is now shaped by a mix of scientific breakthroughs, new technology, and growing clinical needs. It started over 100 years ago when scientists first identified the basic signs of the disease. Since then, we've seen huge advances from basic observations to using hig -tech tools that can catch early changes in the brain. This section looks at how these detection methods have developed over time. It compares the older, more traditional approaches with today's newer technologies and also takes a look at what the future might hold. The discussion is based on key studies and findings from the literature provided.

5.1 Historical Progression of Diagnostic Approaches

Over the past 100 years, the development tools used to detect AD have changed significantly. These changes have come from advances in science, improvements in technology, and shifting priorities in medical care. Those tools have evolved, comparing older diagnostic methods with newer ones, and offering a glimpse into what the future might hold. Based on research from the referenced studies, we can see how AD detection has moved from only being possible after death to more advanced techniques that can spot early signs of the disease sometimes even before symptoms appear giving doctors a better chance to act early.

It all started back in 1906, when Dr. Alois Alzheimer first discovered amyloid plaques and tau tangles in the brain of a patient named Auguste Deter after she died (Hardy & Selkoe, 2002). This was the first time AD was identified as a specific brain disease. After so many years, the doctors could only confirm AD by examining the brain after death, which didn't help much for treating people while they were alive. Things began to change in the mid 1900s when doctors started creating clinical guidelines based on symptoms. Then in the 1980s, cognitive tests like the Mini

Mental State Exam (MMSE) were introduced. These tests helped identify memory and thinking problems in living patients but mostly once the disease was already fairly advanced (Prince et al., 2016).

A major turning point came in the 1990s with the rise of brain imaging. MRI scans made it possible to see physical changes in the brain, such as shrinkage in the hippocampus, a region important for memory (Dubois et al., 2014). In the same time, researchers focused more on the amyloid hypothesis, leading to the development of cerebrospinal fluid (CSF) tests. By the early 2000s, they had identified lower levels of Aβ42 and higher levels of tau in CSF as early signs of AD (Blennow et al., 2010). These advances made it possible to detect AD before serious symptoms appeared (Sperling et al., 2014).

In the 2010s, new imaging tools made things even further. PET scans, using special dyes like Pittsburgh Compound B (PiB) and flortaucipir, allowed doctors to see amyloid and tau buildup in living patients (Villemagne et al., 2013; Bateman et al., 2012). This made it much easier to confirm a diagnosis. In 2018, the National Institute on Aging and the Alzheimer's Association (NIA-AA) updated their guidelines to include these advanced imaging and biomarker tools. They defined Alzheimer's biologically not just by symptoms highlighting the importance of catching the disease early (Jack et al., 2018). Overall, the history of AD detection shows a clear shift like from relying on brain autopsies after death to using live brain scans and lab tests that can spot the disease long before symptoms start. This reflects a growing push toward early intervention, now that we know AD can begin developing many years before people even notice changes in their memory (Sperling et al., 2014).

5.2 Comparison of Traditional vs. Emerging Technologies

Traditional tools for detecting AD like memory tests and early brain scans have played a key role in diagnosing the condition. But now, they're being supplemented by newer technologies that are more sensitive, easier to use, and better at detecting the disease in its very early stages. Tests like the Mini-Mental State Exam (MMSE) and the Montreal Cognitive Assessment (MoCA) are still commonly used because they're simple and low-cost (Prince et al., 2016). But they are not great at picking up on early and subtle changes before symptoms become obvious (Blennow et al., 2010). Similarly, traditional brain scans like structural MRI can spot shrinkage in the hippocampus but only after significant damage has already occurred. So they often miss the very beginning of the disease (Jack et al., 2018).

On the other hand, newer technologies are designed to detect changes at the molecular level and often do that in less invasive ways. For example, PET scans that target amyloid and tau proteins can directly show the brain changes linked to AD, even years before symptoms begin though these scans are still expensive and not widely available (Villemagne et al., 2013; Bateman et al., 2012). Tests that use CSF to measure Aβ42, tau, and p-Tau are very accurate for detecting AD before symptoms show up. But as they require a spinal tap, they're not practical for widespread use (Blennow & Zetterberg, 2018). Blood tests are a promising new step forward as markers like plasma Aβ42/Aβ40 and neurofilament light chain (NfL) could make early screening much easier and more routine, though the results can vary depending on how the tests are done (Sweeney et al., 2018; Klyucherev et al., 2022).

What really sets emerging tools apart is the use of AI and ML which can help analyze all the complex data. AI can spot small changes in MRI and PET scans that human eyes might miss, and

ML can combine data from different biomarkers to improve diagnostic accuracy (Zhang et al., 2022; Kale et al., 2024). Another exciting development is wearable technology devices that track daily behavior and physical changes in real time. These tools offer continuous monitoring, unlike traditional methods that only provide a brief image during a clinic visit (Laske et al., 2015).

While traditional methods are still important and trusted, newer technologies are designed for broader use and earlier detection. Some of these newer tools like saliva and retinal imaging are still need more testing to prove they're reliable (Ausó et al., 2020; Klyucherev et al., 2022). But overall, the trend is moving toward more proactive, accessible, and early diagnosis.

Chapter 6

Future Perspectives and Next-Generation Innovations

Looking forward, the way we detect AD is expected to change in major ways, with a strong focus on making tools more accessible, personalized, fair, and ethically way. New advancements in brain imaging, biomarker testing, and AI have laid a solid foundation for progress. But to fully bring these tools into everyday healthcare and large scale screening, we still need to tackle important gaps and take advantage of new opportunities.

6.1 Standardization and Clinical Integration of Biomarkers

One of the most urgent tasks right now is to create consistent standards for blood-based biomarkers, especially for plasma Aβ42/Aβ40 ratios, NfL, and GFAP. Although correlated strongly with amyloid burden and neurodegeneration, their adoption faces challenges from inter-assay variability and population-specific performance discrepancies (Blennow & Zetterberg, 2018; Kim et al., 2023; Klyucherev et al., 2022). Efforts must establish globally accepted protocols for reliable use in primary and specialized care.

Advances in blood-based biomarkers, particularly plasma Aβ and NfL assays, aim to achieve precision comparable to cerebrospinal fluid (CSF) markers, potentially transforming AD screening into a routine, cost-effective practice similar to cholesterol testing (Sweeney et al., 2018).

Multi-analyte panels combining amyloid, tau, and neuroinflammatory markers also hold promise for enhanced sensitivity and specificity in real-world populations (Guzman-Martinez et al., 2019). Confirmed predictive accuracy from longitudinal studies could transition these panels from research tools to standard clinical tests.

6.2 AI-Driven Precision Diagnostics

AI will play a pivotal role in personalizing AD diagnostics, modeling disease progression, therapeutic responses, and individualized risk profiles (Kale et al., 2024). Developing explainable AI models trusted and interpretable by clinicians in real-time is essential. Models integrating imaging, biochemical data, patient history, environmental exposures, and lifestyle factors will significantly enhance predictive power.

Time-to-event analyses and reinforcement learning frameworks could personalize risk assessment and optimize clinical trial recruitment, identifying high-risk individuals years before symptom onset (Cummings et al., 2021).

Integration of AI with electronic health records (EHRs), neuroimaging software, and wearable technologies will facilitate continuous monitoring and intervention, ensuring seamless functionality within healthcare infrastructures is vital for real-world impact (Zhang et al., 2022). .

6.3 Equity and Dataset Diversity

Equitable AI deployment requires addressing the lack of representation in training datasets, which currently limits generalizability and exacerbates disparities across racial, ethnic, and geographic populations (Ard et al., 2021). Strategic investments in diverse, longitudinal cohort studies, particularly among underrepresented and low-income populations, are critical.

Global harmonization initiatives, including cross-national consortia and open-access biobanks, can enhance data sharing and comparability, ensuring inclusive and equitable care across different health systems (Jack et al., 2018).

6.4 Next-Generation Wearables and Non-Invasive Biomarkers

Wearable technologies represent an evolving frontier for real-time physiological and behavioral monitoring relevant to early AD detection. Embedding validated machine learning algorithms within these devices could track cognitive decline passively through gait, sleep, and speech patterns—data points currently inaccessible (Laske et al., 2015). Long-term validation across diverse populations and real-world settings is critical for clinical reliability (Kulichikhin et al., 2021).

Non-invasive biomarkers, such as salivary tau and retinal amyloid imaging, present exciting prospects. Saliva's ease of collection could democratize screening, and retinal imaging could provide insights into AD via routine eye exams (Ausó et al., 2020; Klyucherev et al., 2022). Validation through multicenter longitudinal studies will be necessary to establish clinical reliability (Guzman-Martinez et al., 2019).

Even though it's still in the early stages, but single cell profiling could help uncover tiny changes in individual cells that can't be seen with broader testing methods. This could give us a better understanding of the very early stages of AD (Kulichikhin et al., 2021).

6.5 Ethical Deployment and Policy Readiness

As the Alzheimer's detection tools become more advanced, the ethical guidelines need to keep up. AI systems that work with personal data like physical measurements, cognitive performance, or behavior must follow strict privacy rules and be managed with transparency (Zhang et al., 2022).

It’s important that people give informed consent before their data is used and that the algorithms are held accountable. Protecting personal information becomes even more crucial as these tools start being used in everyday healthcare and even through at home or consumer based services.

At the same time, policymakers need to make sure healthcare systems are ready to handle these changes. This includes setting up fair ways to cover the costs (reimbursement models) and making sure doctors, nurses, and other health workers are trained to understand biomarker test results and use AI recommendations effectively in patient care (Cummings et al., 2021).

These all innovations are pushing AD away from simply reacting to symptoms and toward preventing the disease before it takes hold. This shift supports the urgent global need for early action and fair access to care for everyone (Brookmeyer et al., 2018; World Health Organization, 2023; Sperling et al., 2014).

Chapter 7

Conclusion

The rapid development of early detection tools for Alzheimer's reflects a significant shift in healthcare toward more preventive, personalized, and data-driven approaches. Previously, diagnoses were largely based on observable symptoms. Today, advances in science and technology allow us to identify changes in the brain long before symptoms emerge (Sperling et al., 2014; Jack et al., 2018). This paradigm shift is transformative, offering individuals the opportunity to begin treatments or implement lifestyle changes at a stage when they can have the greatest effect.

One of the biggest lessons from the research is that using a combination of tools like brain scans, fluid biomarkers, genetic testing, and artificial intelligence that leads to better and more accurate diagnoses (Bateman et al., 2012; Blennow & Zetterberg, 2018; Zhang et al., 2022). When these tools are used together, they don't just confirm the presence of the disease but also help track how far it has progressed and predict how fast it might get worse. This kind of detail helps doctors make smarter, more tailored decisions for each patient.

Early detection also changes how doctors manage the disease. Finding signs of Alzheimer's before symptoms show up gives people the chance to take steps like doing brain exercises, managing heart health, and staying socially active that can slow the disease down (Livingston et al., 2020). These strategies work best when started early before the brain experiences major damage which is why early and accurate detection is so important.

This review also makes it clear that the healthcare system itself needs to be ready. As tools like blood tests and AI powered diagnostics get closer to being used in everyday clinics, we'll need to train healthcare workers, upgrade medical facilities, and put strong ethical policies in place (Cummings et al., 2021; Kale et al., 2024). Without this kind of preparation, these breakthroughs

might only benefit a few specialized centers—leaving out many people, especially those in under-resourced areas (Brookmeyer et al., 2018; World Health Organization, 2023).

Even though we still don't have a cure for AD, but early detection offers real hope. It opens doors for people to join clinical trials sooner, make informed choices about their lives, and possibly delay the need for full time care. With AD cases expected to rise globally and the message is clear: investing in early detection isn't just good medicine it's the right thing to do for society as a whole (Prince et al., 2016; Ard et al., 2021).

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