# PRO - YOU
# PROJECT

## *OVERVIEW OF USE CASES*

**by**

**CSP TELEMEDICINE** ***Care Save prevent***

**SECTIONS**

***Introducing the CSP Telemedicine Care Save Prevent Medical Tracker Device***

DISEASES AND NUMBERS

FROM USE CASE TO CONSUMER

RESEARCH & OUTCOME

PATIENTS, CAREGIVERS AND PHYSICIANS

THE DEVICE

THE ALGORITHMS

REIMBURSEMENT

SYNERGIES:

- -PHARMACEUTICAL
- -COMPANIES
- -INSURANCES
- -ASSOCIATIONS

GRANT

OVERVIEW OF USE CASES

FROM DEMENTIA TO EPILEPSY AND MORE

*Thanks to specific features and algorithms for long lasting batteries, the Alzheimer's was our main target in building a medical tracker device. The Market is really interested, and ready to go.*

*On closer inspection, nevertheless, we understood to have the complete ability to go forward.*

*Thanks to further dedicated algorithms, the expertise and knowledge of Motion Laws, applied to clinical issues, allow us to intend the use of this medical devices for all the cases in which movement changes make the difference, in a complete lack of medical devices intended for monitoring and studying neurological diseases.*

Premises.

1. *There aren't at now medical devices, clinically tested, able to track the movements and the habits of people suffering from neurological pathologies, to observe and study surely the outcomes of therapies or clinical trials, to help strongly the caregivers of patients suffering from e.g. Dementia or Autism (coming lost, wandering, elopement).*

2. *The Medical device is intended for:*
    a. *Dementia incl. Alzheimer's:* *Caregiver, Hospital*
    b. *Parkinson's:* *Neurologist, Hospital, Patient*
    c. *Parkinsonism:* *Neurologist, Hospital, Patient*
    d. *Epilepsy:* *Caregiver, Hospital, Neurologist, Patient*
    e. *Autism:* *Caregiver, Neurologist, Psychologist, Patient*
    f. *Sleep disturbance:* *Neurologist, Psychologist, Hospital, Patient*
    g. *MS, Para paresis, MD:* *Neurologist, Hospital, Patient*
    h. *Post neurosurgery:* *Neurologist, Neurosurgeon, Hospital, Patient*
    i. *Post Stroke - Rehab:* *Neurologist, Hospital, Physical Therapies, Patient*

3. *The medical tracker device we built in MR&D works as gateway coupled with more devices.*

## THE NUMBERS

| DISEASE | AFFECTED POPULATION & COST / Y<br>CDC.GOV- ASSOCIATIONS |
|---|---|
| **DEMENTIA**<br>*Only on Alzheimer's, that is the 70-80% of all the Dementia* | ITA 1.241.000 (260.000 new patients/y) – 37 BILL<br>U.S.A 9.400.000 – 226 BILL<br>Europe 10.500.000 PATIENTS<br>Worldwide cost: 818 BILL (ESTIMATED 1 TRILLION IN 2018 WITH 140.000.000 PATIENTS IN 2050). |
| **(MCI)** | THEY ARE THE PATIENTS WHO WILL DEVELOP DEMENTIA |
| **PARKINSON'S**<br>*Many undetected cases* | ITA 250.000<br>U.S.A 1.000.000 (60.000 new patients/y) – 25 BILL<br>Europe 1.000.000 PATIENTS<br>Worldwide 10.000.000 PATIENTS |
| **EPILEPSY** | ITA 500.000<br>U.S.A 3.000.000 – 15.5 BILL<br>Europe 6.000.000<br>Worldwide 50.000.000 PATIENTS |
| **AUTISM** | ITA 880.000 –<br>U.S.A 3.500.000 – ONLY FOR CHILDREN: FROM 11 TO 60.9 BILL, av > 35 BILL |
| **SLEEP DISTURBANCE** | ITA 7- 10.000.000<br>U.S.A 50-70.000.000<br>*WHERE POLYSOMNOGRAPHY IN ITALY COSTS FROM 200 (AT HOME) TO 2.000 USD IN HOSPITAL FOR NARCOLEPSY, PARASOMINA, SOMNAMBULISM* |
| **STROKE** | ITA 200.000 – 14.5 BILL<br>U.S.A 800.000 – 36.5 BILL<br>Worldwide 15.000.000 PATIENTS |
| **MS** | 1.000.000 WORLDWIDE (0,07%) |
| **MD** | 0,013% OF PEOPLE WORLDWIDE |

*Global cost for these diseases in US (except Sleep Disturbance: no data): > 330 BILL per year.*

## THE DEMENTIA

Dementia is incorrectly referred to "senility": the mental decline is not a normal part of aging, although the greatest known risk factor is increasing age, and the majority of people with Alzheimer's are 65 and older. Up to 5 percent of people with the disease have early onset Alzheimer's ("younger-onset"), which often appears when someone is in their 40s or 50s.

It is wide range of symptoms, frequently associated with a decline in memory or other thinking skills severe enough to reduce a person's ability to perform everyday activities. Alzheimer's disease accounts for 70 - 80 percent of cases. Vascular dementia, which could occur after a stroke, is the second most common Dementia type. Few conditions of Dementia could be reversible.

## 1. ALZHEIMER'S

**LONG TERM REMOTE MONITORING**

| | PRESENT | CSP - MR&D MD |
|---|---|---|
| **DEVICES** | Trackers from the Market.<br>Derivation from cellular phone technology.<br>Accelerometer, GPS. | Medical device clinically tested, water and shock proof. Long life battery thanks to specific algorithms. Virtual static and dynamic fence.<br>Alerts. |
| **NOTES** | Not clinically tested.<br>No long life battery.<br>No water-shockproof.<br>No automatic alerts. | Absolute reduction of risk of wandering, elopement, going lost.<br>Behavior monitoring.<br>Less use of medicines.<br>Better quality life of patient and caregiver and reduction of seriousness of disease.<br>Remote monitoring of trend of disease or related diseases (many have also P or epileptic seizures).<br>Save money. |

| | |
|---|---|
| KEY DRIVERS | Innovation<br>Saving money<br>Alzheimer's Association<br>Ministry of Health<br>Insurances<br>Physicians |

Alzheimer's is a progressive disease, where dementia symptoms gradually worsen over a number of years. In its early stages, memory loss is mild, but with late-stage Alzheimer's, individuals lose the ability to carry on a conversation and respond to their environment. Alzheimer's is the sixth leading cause of death in the United States.
Although current Alzheimer's treatments cannot stop Alzheimer's from progressing, they can temporarily slow the worsening of dementia symptoms and improve quality of life for those with Alzheimer's and their caregivers. Today, there is a worldwide effort under way to find better ways to treat the disease, delay its onset, and prevent it from developing.

People with dementia may have problems with short-term memory, keeping track of a purse or wallet, paying bills, planning and preparing meals, remembering appointments or traveling out of the neighborhood.
Many dementias are progressive, meaning symptoms start out slowly and gradually get worse.

OVERVIEW OF DISEASE PROGRESSION & THE CAREGIVER FUNCTION

The symptoms of Alzheimer's disease worsen over time, although the rate at which the disease progresses varies. Depending on other factors, a person with Alzheimer's lives four to twenty years after diagnosis.

Changes in the brain related to Alzheimer's begin years before any signs of the disease. This time period, which can last for years, is referred to as preclinical Alzheimer's disease.

1. Mild Alzheimer's disease (or early-stage)
The patient may still drive, work and be part of social activities. Despite this, the person may feel as if he or she is having memory lapses, such as forgetting familiar words or the location of everyday objects. Common difficulties include problems coming up with the right word or name, trouble remembering names when introduced to new people, having greater difficulty performing tasks in social or work settings, forgetting material that one has just read, losing or misplacing a valuable object, increasing trouble with planning or organizing.
The early stages of Alzheimer's can last for years.
A person may function independently.

A person in the early stages may experience mild changes in the ability to think and learn, but he or she continues to participate in daily activities and give-and-take dialogue. To others, the person may not appear to have dementia.
The *caregiver role* is of support, love and companionship, to help with daily life, as needed, and to help the person with Alzheimer's plan for the future.
A person with early-stage Alzheimer's may need cues and reminders to help with memory. For example, he or she may need help with keeping appointments, remembering words or names, keeping track of medications
Is very important the patient continues living as independently as possible.
The caregiver can help the person stay organized with shared calendars, notes, medication schedules and other reminder systems. Establishing a daily routine and maintaining some regularity will be of benefit. The person also will need emotional support. He or she may feel frustrated, anxious, embarrassed or isolated.

2. Moderate Alzheimer's disease (or middle-stage)
This is typically the longest stage and can last for many years. As the disease progresses, the person with Alzheimer's will require a greater level of care.
The person with Alzheimer's confuses words, gets frustrated or angry, or acts in unexpected ways, such as refusing to bathe. Damage to nerve cells in the brain can make it difficult to express thoughts and perform routine tasks.

At *this point, symptoms will be noticeable to others and may include forgetfulness of events or about one's own personal history, feeling moody or withdrawn, especially in socially or mentally challenging situations, being unable to recall their own address or telephone number or the high school or college from which they graduated, confusion about where they are or what day it is, the need for help choosing proper clothing for the season or the occasion, trouble controlling bladder and bowels in some individuals, changes in sleep patterns, such as sleeping during the day and becoming restless at night, an increased risk of wandering and becoming lost.*
*Personality and behavioral changes, including suspiciousness and delusions or compulsive, repetitive behavior like hand-wringing or tissue shredding.*

During the middle stages of Alzheimer's, damage to the brain can make it difficult to express thoughts and perform routine tasks.
Being a caregiver for someone in the middle stages of Alzheimer's requires flexibility and patience. As the abilities of the person with Alzheimer's change, and functioning independently becomes more difficult, the caregiver will have to take on greater responsibility. Daily routines will need to be adapted, and structure will become more important.
When abilities diminish further, habits will need to be modified.
The caregivers have to take care of themselves taking breaks, even if it is only for a few moments.

3. Severe Alzheimer's disease (late-stage)
In the final stage of this disease, individuals lose the ability to respond to their environment, to carry on a conversation and, eventually, to control movement. They may still say words or phrases, but communicating pain becomes difficult. As memory and cognitive skills continue to worsen, personality changes may take place and individuals need extensive help with daily activities.
At this stage, individuals may require full-time, around-the-clock assistance with daily personal care, lose awareness of recent experiences as well as of their surroundings, require high levels of assistance with daily activities and personal care, experience changes in physical abilities, including the ability to walk, sit and, eventually, swallow and have increasing difficulty communicating.

The late stage of Alzheimer's disease may last from several weeks to several years. As the disease advances, intensive, around-the-clock care is usually required.
As the disease advances, the needs of the person living with Alzheimer's will change and deepen. A person with late-stage Alzheimer's usually has difficulty eating and swallowing, needs assistance walking and eventually is unable to walk, needs full-time help with personal care, is vulnerable to infections, especially pneumonia, loses the ability to communicate with words.

EPIDEMIOLOGY & PUBLIC COST OF THE DISEASE
*World Health Organization – Alzheimer Association 2015*

Every 3 seconds there is worldwide a new diagnosis of Dementia (10.000.000 new cases in 2015).

This year in Italy there are 1.241.000 patients (with 260.000 new patients/y);
In Europe 10.500.000 patients. In U.S.A 9.400.000, Asia ed Australia 23.000.000, Africa 4.000.000

In Italy we spend 37 bil USD/y, in USA 226 USD bil/y. Worldwide 818 bil USD (2015), estimated 1 tril USD in 2018 and 2 tril USD in 2030.
The cost are in continuous progress: the patients worldwide suffering from Dementia, including Alzheimer' are estimated to be 140.000.000 in 2050.

## *HOW OUR DEVICE WORKS*

In our intention, the medical device needs to work for many weeks without charging batteries.
So we worked on technical features and algorithms and we designed innovative virtual fences.

1. The medical device is coupled with a beacon (long battery life, estimated 24 months) that emits signals captured from the device. The GPS module is turned OFF.
Into this fence the device tracks movements thanks to gyroscope and 6 axis accelerometer. We

defined three concentric increasing fences. The data are transmitted to servers once a day.

The fence as allowed from the beacon is:

a. Static. At home or Hospital
b. Dynamic. When the caregiver and the patient are together, the GPS module is turned OFF. When the patient goes out the fence established from beacon, the GPS module turns ON.

When the patient is pout from fence, we define a point *"zero"* on MAP, describing one more fence of 1/3 miles diameter (500 meters). We design static points (the address of the patient) and dynamic points (knowing the point "zero" and the address).

Alerts. They arrive to the smartphone of the caregivers (and

1. *Wandering.* When the patient wanders versus the beacon under the logic of specific algorithms, the caregiver receives on the smartphone ***ALERT WANDERING.*** *A "bonus malus theory" assigns values for repetitive or new behaviors deciding transmitting or not the alert).*

2. *Elopement.*

*a. The patient goes away from the point zero (and beacon=caregiver).* ***ALERT POSSIBLE ELOPEMENT.***

b. The patient goes out from the 1/3 miles fence. ***ALERT ELOPEMENT.***

c. The patient goes away speedly (on car, bus). ***ALERT BULLISH ELOPEMENT***.

d. The patient goes toward own home. ***ALERT ELOPEMENT TOWARD HOME***.

3. *Going o getting lost.* The patient escapes more than 1,2 miles (2 Kilometers) from the point "zero", ***ALERT GOING LOST.*** The internal logic saves energy.

4. *Become lost*: by time and distance from point "zero" (2 miles, or 3 Kilometers). ***ALERT BECOME LOST.*** Only GPS module ON, the position is notified with growing time. When the battery level is <5%, the device transmits the last signal: ***ALERT BECOME LOST - BATTERY !!!***

MAIN TARGET – INTENDED USE

We estimated the mild and moderate disease amount at least the 90% of all the patients suffering from Alzheimer's.

Our device was built and designed for tracking and monitoring:

-50 to 60 % mild disease
-100 % moderate disease
-20 % severe disease depending from autonomy and familiar status

of the patients suffering from Alzheimer's.

## MCI

The Middle Cognitive Impairment is a prodromal stage of Alzheimer's disease where the first clinical symptom is memory loss.
We know from clinical evidences and scientific literature the patients have a delay of several years in the occurrence of the event of major illness if they are active and with a better lifestyle.

Our proposal, clinically discussed, is to study under Horizon 2020 with the Carlo Besta Neurological Institute, worldwide Universities and the Alzheimer's Associations, 300 patients across three to five years compared to 300 patients without our device, tracking the daily activities and habits to understand how to go forward (primary end secondary prevention).

We have no data on MCI depending from to many parameters and so poor epidemiology.

INTENDED USE
With clinical data evidence, to be prescript from Neurologist to patients suffering from evidence of memory loss.
It would be used for long time (many years) to reduce the major illness, thanks to the continuous monitoring of the trend of disease and behavior, changing habits.

**PARKINSON'S**

*The Parkinson's Disease Foundation – The Michael J Fox Foundation*

This progressive disorder of the nervous system affects essentially the *movement*. It develops gradually, sometimes starting with a barely noticeable tremor in just one hand. But while a tremor may be the most well-known sign of Parkinson's disease, the disorder also commonly causes stiffness or slowing of movement.
Although Parkinson's disease can't be cured, correct medications may markedly improve the symptoms. Parkinson's disease symptoms and signs may vary from person to person and may include tremor, bradykinesia, muscle stiffness, impaired posture and balance, loss of automatic movements, speech and writing changes.

EPIDEMIOLOGY & COSTS
*The Parkinson's Disease Foundation – The Michael J Fox Foundation – CDC.gov*

In Italy 250.000 patients suffer from Parkinson's, 1 million in Europe, 1 million in U.S.A, estimated 10 million in the world.
Approximately 60,000 Americans are diagnosed with Parkinson's disease each year, and this number does not reflect the thousands of cases that go undetected.
Incidence of Parkinson's increases with age, but an estimated four percent of people with PD are diagnosed before the age of 50.
The combined direct and indirect cost of Parkinson's, including treatment, social security payments and lost income from inability to work, is estimated to be nearly $25 billion per year in the United States alone.

## 2. PARKINSON'S

**LONG TERM REMOTE MONITORING**

| | PRESENT | CSP - MR&D MD |
|---|---|---|
| **DEVICES** | N.A. | Medical device clinically tested. Thanks to specific algorithms allows remote monitoring of myoclonic movement, pill rolling, resting tremor, muscle stiffness, postural and balance instabilities and impaired coordination, freezing, behavior change |
| **NOTES** | N.A. | Remote monitoring of trend of disease or related diseases (many have also sleep disturbances or epileptic seizures and behavioral disorders).<br>Clinical outcome.<br>Therapies evaluation.<br>Synergie e.g. with GONDOLA |

| | |
|---|---|
| KEY DRIVERS | Innovation<br>Pharma<br>Parkinson's Association worldwide, Michael J Fox Association (MJFF)<br>Insurances<br>Physicians |

HOW OUR DEVICE WORKS & INTENDED USE

Thanks to MEMS, functions and specific algorithms on board and on server, our device allows to *remote monitoring* myoclonic *movement*, pill rolling and resting tremor, muscle stiffness, postural and balance instabilities and impaired coordination, speed of arm movement and related alterations, freezing, speed of motion (walking) and related alterations, amount and quality (fluidity-degree of difficulty) of movement and related changes, difficulty (degree) in getting up (with number of attempts), amount of hours lived in bed or on a chair, sleep disturbances, fall down, and moreover *to allow the validation of therapies, the outcomes of new therapies, and the trend of the disease.*

The device, mainly intended for Physicians, allows efficaciously to remote monitoring motor and behavioral abnormalities and related movements disturbances, the differential diagnosis for Parkinson's and parkinsonism, to adjust the right medical therapy (when, how many time), to validate new therapies and scientific outcomes.

The data on platform allow the Physicians to monitor the trend of the disease and the effectiveness of medicines.

**AUTISM**

*CDC.gov – National Autism Association (USA)*

Autism spectrum disorder (ASD) is a developmental disability that can cause significant social, communication and behavioral challenges. There is often nothing about how people with ASD look that sets them apart from other people, but people with ASD may communicate, interact, behave, and learn in ways that are different from most other people. The learning, thinking, and problem-solving abilities of people with ASD can range from gifted to severely challenged. Some people with ASD need a lot of help in their daily lives; others need less.
A diagnosis of ASD now includes several conditions that used to be diagnosed separately: autistic disorder, pervasive developmental disorder not otherwise specified (PDD-NOS), and Asperger syndrome. These conditions are now all called autism spectrum disorder.
People with ASD often have problems with social, emotional, and communication skills. They might repeat certain behaviors and might not want change in their daily activities. Many people with ASD also have different ways of learning, paying attention, or reacting to things. Signs of ASD begin during early childhood and typically last throughout a person's life.
Children or adults with ASD might have social impairments, cognitive impairments, communication difficulties, and repetitive behaviors.

Because Autism is a spectrum disorder, it can range from very mild to very severe and occur in all ethnic, socioeconomic and age groups. Males are four times more likely to have autism than females. Some children with autism appear normal before age 1 or 2 and then suddenly "regress" and lose language or social skills they had previously gained. This is called the regressive type of autism.

## 3. AUTISM

**LONG TERM REMOTE MONITORING**

| | PRESENT | CSP - MR&D MD |
|---|---|---|
| **DEVICES** | N.A. | Medical device clinically tested, water and shock proof. Long life battery thanks to specific algorithms. Virtual static and dynamic fence. Alerts. |
| **NOTES** | N.A. | Absolute reduction of risk of wandering, elopement, going lost.<br>Behavior monitoring.<br>Better quality life of patient and caregiver.<br>Remote monitoring of trend of disease.<br>Save money. |

| | |
|---|---|
| KEY DRIVERS | Innovation<br>Pharma<br>Autism Association worldwide<br>US and Italian Ministry of health<br>Insurances<br>Physicians<br>Companies. Automatically opposite sounds against noises producing behavioral abnormalities |

According to a 2012 study in Pediatrics, 49% of children with ASD have a tendency to wander or bolt from safe settings. Individuals with ASD are often attracted to water, yet have little to no sense of danger. Drowning is a leading cause of death in children with ASD.
*ASD wandering behaviors happen under every type of supervision* and are usually a form of communication — an "I need," "I want," or "I don't want." Individuals with ASD will wander or bolt to get to something of interest, or away from something bothersome.
*Nearly half of children with autism engage in wandering behavior*; increased risks are associated with autism severity; more than one third of children with autism who wander/elope are never or rarely able to communicate their name, address, or phone number; accidental drowning accounts for approximately 90% of lethal outcomes.

Other dangers include dehydration; heat stroke; hypothermia; traffic injuries; falls; physical restraint; encounters with strangers.

EPIDEMIOLOGY & COSTS
*CDC.gov – National Autism Association – Autism Society (USA)*

More people than ever before are being diagnosed with ASD. It is unclear exactly how much of this increase is due to a broader definition of ASD and better efforts in diagnosis. However, a true increase in the number of people with an ASD cannot be ruled out. We believe the increase in ASD diagnosis is likely due to a combination of these factors.

It's estimated that 1,47 % of people, or one out every 68 individuals (*focused on children 8 years old*) has an Autism Spectrum Disorder (ASD).

More than 3.5 million Americans live with an autism spectrum disorder.

The total costs per year for children with ASD in the United States were estimated to be between $11.5 billion - $60.9 billion (2011 US dollars). This significant economic burden represents a variety of direct and in-direct costs, from medical care to special education to lost parental productivity.

In 2005, the average annual medical costs for Medicaid-enrolled children with ASD were $10,709 per child, which was about six times higher than costs for children without ASD ($1,812). In addition to medical costs, intensive behavioral interventions for children with ASD cost $40,000 to $60,000 per child per year.

Expenses for each autistic person with an intellectual disability may be $2.4 million in the U.S. and $2.2 million in the U.K., largely driven by the costs of residential care, special education and reduced employment prospects. For those who don't have an intellectual disability, costs are estimated to be about $1.4 million per person in both countries, according to a study published in JAMA Pediatrics.

The cost of supporting children with autism is estimated to be $61 billion to $66 billion a year in the U.S. and $4.5 billion to $5 billion a year in the U.K., depending on how many people it was projected had an intellectual disability. For autistic adults, the costs were $175 billion to $196 billion a year in the U.S. and $43 billion to $46 billion a year in the U.K.

HOW THE DEVICE WORKS.

*See Alzheimer's for definition of fence and alerts.*

*The behavioral impairment are defined by movement changes detected from the device and processed by specific algorithms.*

INTENDED USE

The device is intended for:

1. Physicians. It allows to:
    a. remote monitoring running, social impairment, rocking body, spinning in circle, hyperactivity, unusual sleeping habits
    b. test the outcomes of new or experimental therapies
    c. monitor the trend of the disease during the time.

2. Caregivers: specific algorithms are designed for an easy, virtual interactive geofencing through MAP with prompt elopement – wandering – coming lost alert.

*It means more serenity and saving money.*

SEE ATTACHED:
A NEW MECHANICAL THERAPY THE AUTISM, THE EPILEPSY& THE NOISE
FROM THE ADVERSE EVENT TO THE ACTIVE NOISE CONTROL

**EPILEPSY**

*The Epilepsy Foundation & Centers for Disease Control and Prevention CDC.gov*

Epilepsy is a spectrum condition with a wide range of seizure types and control varying from person-to-person, and it is the 4th most common neurological problem – only migraine, stroke and Alzheimer's disease occur more frequently.
It can be caused by different conditions that affect a person's brain, like stroke, tumor, traumatic injury, central nervous system infections. Many times the cause is unknown.
Epilepsy can be a chronic disorder, the hallmark of which is recurrent, unprovoked seizures. Many people with epilepsy have more than one type of seizure and may have other symptoms of neurological problems as well. Sometimes EEG testing, clinical history, family history and outlook are similar among a group of people with epilepsy. In these situations, their condition can be defined as a specific epilepsy Syndrome.
The location of that event, how it spreads and how much of the brain is affected, and how long it lasts all have profound effects. These factors determine the character of a seizure and its impact on the individual.
Having seizures and epilepsy can also affect one's safety, relationships, work, driving and so much more.

## 4. EPILESPY

**IN HOSPITAL MONITORING – AT HOME LONG TERM REMOTE MONITORING**

| | PRESENT | CSP - MR&D MD |
|---|---|---|
| **DEVICES** | AT HOSPITAL<br><br>EEG | Medical device clinically tested, water and shock proof. Remote monitoring of epileptic seizures (when, where, how long, type). |
| **NOTES** | N.A. | Better quality life of caregiver.<br>Remote monitoring of trend of disease.<br>Therapies validation.<br><br>Hospital. Prevention System, remote monitoring of all neurological patients.<br>At home. Remote monitoring of people suffering from. |

| | |
|---|---|
| KEY DRIVERS | Innovation<br>Epilepsy Association – US Ministry of Health<br>Physicians<br>Pharma<br>Synergies: detecting and automatic at home production of sounds against typical behavioral crisis. |

EPIDEMIOLOGY & COSTS
*The Epilepsy Foundation - CDC.gov*

In U.S.A., according to the latest estimates, about 1% of adults aged 18 years or older (about 2.4 million) have *active* epilepsy.
About 0.6% of children aged 0-17 years (460,000) have active epilepsy.
*(About 1.8% of adults aged 18 years or older (4.3 million) have had a diagnosis of epilepsy or seizure disorder. About 1% of children aged 0-17 years (750,000) have had a diagnosis of epilepsy or seizure disorder).*

The total indirect and direct cost of epilepsy in the United States is estimated to be $15.5 billion yearly.

In Italy 500.000 patients suffer from epilepsy, 6 million in Europe, 50 million in the world.

The 70% of patients respond to medical therapy.
The 10% of patients is candidate to surgical intervention on the brain trigger zone.

HOW IT WORK & INTENDED USE

Thanks to specific algorithms, the device allows to remote monitoring seizures (kind of wave, where, when, how long, differential diagnosis), the adjusting and/or validation of therapies, the outcomes of new therapies, and the trend of the disease.

*This kind of information is very important for Physicians.*
*A prompt alert of a seizure is reassuring Caregivers about the health condition of the loved, inside or outside home, mainly when parents of children aged 1-14.*

*Future option. To connect the tracker become gateway to a 12 sensors for Electro Encephalogram having for the first time a prolonged "like-Holter" exam.*

***Suggested link and comment.***
http://www.epilepsy.com/get-help/managing-your-epilepsy/tracking-my-seizures/importance-tracking-seizures

*Our medical tracker substitutes the diaries, and let Physicians to have real outcomes.*

http://ghr.nlm.nih.gov/condition/autosomal-dominant-partial-epilepsy-with-auditory-features
People with epilepsy could have seizure for noises.
See the attached:
A NEW MECHANICAL THERAPY THE AUTISM, THE EPILEPSY& THE NOISE
FROM THE ADVERSE EVENT TO THE ACTIVE NOISE CONTROL

## SLEEP DISTURBANCE

*ASA American Sleep Association –*
*CDC.gov http://www.cdc.gov/nchs/nhis.htm*
*National Health Interview Survey, 2012 - USA*

Sleep is increasingly recognized as important to public health, with sleep insufficiency linked to motor vehicle crashes, industrial disasters, and medical and other occupational errors. Unintentionally falling asleep, nodding off while driving, and having difficulty performing daily tasks because of sleepiness all may contribute to these hazardous outcomes. Persons experiencing sleep insufficiency are also more likely to suffer from chronic diseases such as hypertension, diabetes, depression, and obesity, as well as from cancer, increased mortality, and reduced quality of life and productivity.

Sleep insufficiency may be caused by broad scale societal factors such as round-the-clock access to technology and work schedules, but sleep disorders such as insomnia or obstructive sleep apnea also play an important role.

An estimated 50-70 million US adults have sleep or wakefulness disorder.

## 5. SLEEP DISORDERS

**IN HOSPITAL AND AT HOME REMOTE MONITORING**

| | PRESENT | CSP - MR&D MD |
|---|---|---|
| **DEVICES** | (VIDEO) POLYSOMNOGRAPHY<br><br>ACTIGRAPHY | Medical device clinically tested. Coupled with BodyGuardian and oximeter, remote monitoring of: daily and night-time movement activity, body activity and position, insomnia, narcolepsy, Restless Legs Syndrome, breath rate, ECG, oximetry, snoring record.<br>Monitoring of related behavior abnormalities or disease. |
| **NOTES** | Obsolete and very expensive exam, barely sustained from patients, misrepresented | Remote monitoring of trend of disease.<br>Therapies validation. |

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|---|---|
| KEY DRIVERS | Innovation and substitution of polysomnography<br>Sleep Disorders Association – Hospitals – Medical Centers<br>Physicians<br>Pharma<br>Synergies: gateway for BodyGuardian, EEG, oximetry, CPAP and more |

A CLINIC OVERVIEW

*Insomnia* is characterized by an inability to initiate or maintain sleep. It may also take the form of

early morning awakening in which the individual awakens several hours early and is unable to resume sleeping. Difficulty initiating or maintaining sleep may often manifest itself as excessive daytime sleepiness, which characteristically results in functional impairment throughout the day.

*Narcolepsy*. Excessive daytime sleepiness (including episodes of irresistible sleepiness) combined with sudden muscle weakness are the hallmark signs of narcolepsy. The sudden muscle weakness seen in narcolepsy may be elicited by strong emotion or surprise. Episodes of narcolepsy have been described as "sleep attacks" and may occur in unusual circumstances, such as walking and other forms of physical activity.

*Restless Legs Syndrome (RLS)* is characterized by an unpleasant "creeping" sensation, often feeling like it is originating in the lower legs, but often associated with aches and pains throughout the legs. This often causes difficulty initiating sleep and is relieved by movement of the leg, such as walking or kicking.

*Sleep Apnea*. Snoring may be more than just an annoying habit – it may be a sign of sleep apnea. Persons with sleep apnea characteristically make periodic gasping or "snorting" noises, during which their sleep is momentarily interrupted. Those with sleep apnea may also experience excessive daytime sleepiness, as their sleep is commonly interrupted and may not feel restorative.

*Somnambulism*. Sleepwalkers can perform activities that are usually performed during a state of full consciousness, till walking to a bathroom, and cleaning, or as hazardous as cooking.
In the "true insomnia" the can drive for many miles or make violent gestures.
INTENDED USE

HOW IT WORK & INTENDED USE
Thanks to specific algorithms, We want to substitute the polysomnography (or the to much poor of information actigraphy) with a representative of real 24 h remote monitoring at home with CSP medical device, Body Guardian and oximetry.

We can easily monitor:
-daily and night-time movement activity
-hours lived on chair or bed
-body activity and position into the bed
-insomnia - narcolepsy
-Restless Legs Syndrome
-breath rate
-ECG
-oximetry
-snoring record

We designed clinical trials to test the effectiveness of our solution vs the polysomnography.
The powered capability of the matched devices during an at home living vs the into hospital monitoring with bends, cables, and so on, will be disruptive, allowing to Physicians to validate therapies, monitoring epileptic seizures, parasomnic events, insomnia, narcolepsy, sleep apnea, RLS and more.
This kind of architecture can enterprise new frontiers for Pharma Industries and Physicians in monitoring patients suffering from sleep disorders.

One more opportunity is to complete the offer with the portable *EEG monitoring* and *CPAP* exam.

## STROKE

Stroke is the third cause of death (12% of all the deaths) after Ischemic myocardial attack (IMA) and cancer. It is the first cause of disability. 15 million people worldwide suffer from stroke every year, commonly for atrial fibrillation (AF). The prevalence increases with the age, in a increasingly ageing population where >10% of over-80s has AF.

## 6. STROKE

**LONG TERM REMOTE MONITORING**

| | PRESENT | CSP - MR&D MD |
|---|---|---|
| **DEVICES** | N.A. | Medical device clinically tested. Remote monitoring of the trend of disability in people suffering from the effects of a stroke and the progresses e.g. of rehabilitation program, as well to detect fall down or epileptic seizures.<br>Monitoring of related behavior abnormalities or disease. |
| **NOTES** | N.A. | Remote monitoring of trend of disease.<br>Therapies validation.<br>Detection of new stroke, recurrent in 25% of people. |

| | |
|---|---|
| KEY DRIVERS | Innovation<br>Hospitals – Medical Centers - Caregivers<br>Physicians<br>Pharma<br>Insurances<br>Rehab |

| COUNTRY | STROKES | EMBOLIC STROKES | DEATH | LIVING WITH EFFECTS | GLOBAL COST * |
|---|---|---|---|---|---|
| **USA** | **800.000** | **125.000** | **130.000** | **610.000** | **36,5 USD BILL** |
| **UK** | **110.000** | **50.000** | **60.000** | **900.000** | **10 BILL** |
| **FRANCE** | **NO RECENT DATA** | **-** | **-** | **-** | **8 BILL + INS** |
| **NEW ZEALAND (pop 4.400.000)** | **6.000** | **2.000** | **3.000** | **(5 YEARS MONIT. FOLLOW-UP)** | **450 MILL (2015 700 MILL)** |
| **ITALY** | **200.000** | **50.000** | **65.000** | **930.000** | **14,5 BILL** |

GLOBAL COST INCLUDES: LOST PRODUCTIVITY, DISABILITY, CAREGIVING ETC

The 25% of Strokes are recurrent, 87% ischemic, 20% fatal, 36% in individual aged > 80.

The Stroke represents the 20% of all the "acute hospital beds" and the 25% of "long-term beds".

These numbers increase for 5-8%/Y.

HOW IT WORKS & INTENDED USE

Thanks to specific algorithms, we are able to monitor the trend of disability in people suffering from the effects of a stroke and the progresses e.g. of rehabilitation program, as well to detect fall down or epileptic seizures.

It is universally recognized (WHO and scientific literature evidence) the fast intervention (STROKE-UNIT) on patients reduce strongly the prevalence of death and the long-term effects of disability in patients for any reason monitored or in the recurrent stroke.

## MULTIPLE SCLEROSIS

CDC.gov

**The Prevalence of Multiple Sclerosis in 3 US Communities**

Noonan CW, Williamson DM, Henry JP, Indian R, Lynch SG, Neuberger JS, et al. The prevalence of multiple sclerosis in 3 US communities. Prev Chronic Dis 2010;7(1):A12

Multiple sclerosis (MS) is an inflammatory demyelinating disease of unknown origin; it affects **more than 1 million people worldwide** (0,07% of people) and disproportionately affects women and whites. It can range from relatively benign to somewhat disabling to devastating, as communication between the brain and other parts of the body is disrupted. Approximately 85% of affected people have a relapsing-remitting course, characterized by an unpredictable course of exacerbations and remissions. Ultimately, most patients become disabled and may or may not have superimposed relapses (secondary progressive MS). Approximately 15% of patients have primary progressive MS, in which the condition worsens gradually from disease onset and is not associated with relapses.

## MUSCLE DYSTROPHY

CDC.gov

Muscular dystrophies are a group of diseases caused by defects in a person's genes. Over time, this muscle weakness decreases mobility and makes the tasks of daily living difficult. There are many muscular dystrophies that affect specific groups of muscles, have a specific age when signs and symptoms are first seen, vary in how severe they can be, and are caused by imperfections in different genes. Muscular dystrophy can run in the family, or a person might be the first one in their family to have the condition.
Muscular dystrophy is rare, the overall prevalence is 1,38 per 10.000 males with Duchenne and Becker MD, the more diffused one type.

## SPASTIC PARA-PARESIS, POST NEUROSURGERY REHAB

*To be completed for lack of official data.*

## THE CSP MEDICAL DEVICE & SERVICE

PATIENTS
CAREGIVERS AND PHYSICIANS

## THE PATIENT

The intended use of the device is not directly designed for Patients, although those are suffering from MCI or very mild cognitive impairment (where a greater activity level or better quality life can improve health), sleep disturbance, or are in rehab program, could meet a personal quality life related improvement.
Nevertheless, all the patients that are remote monitored through our device will benefit from freedom, self-confidence, better therapies program, clinical outcome evidences, and finally better quality life.

## THE CAREGIVERS

*World Health Organization – Alzheimer Association – Gallup - RAND Corporation study, 2013 - MetLife - The Caregiver Foundation – Amherst H Wilder Foundation - National Alliance for Caregiving and Evercare Foundation*

*Many neurological diseases like Alzheimer's, Autism, Epilepsy, morally and practically impose a (various) check of the loved.*

In US nearly 10 million adults are caring for older parents. The unpaid care they provide is estimated to be worth $375 billion dollars per year in a report by Indiana University.
Caregivers clearly take on their heroic role out of love and duty, but for many, cost is also a big part of the equation. A lot of caregivers believe that caring for aging parents themselves is more affordable than professional senior care. After all, the logic goes, assisted living communities and nursing homes are quite expensive, so it must be cheaper to do it yourself.

But this is often a miscalculation. *There are many clouded costs* to family caregiving that should be considered before committing to becoming the full-time caregiver for an older loved one. Being aware of these costs can also help non-caregivers appreciate the sacrifice caregivers make, and the profound importance of their role.

a. Leaving job. Family caregivers frequently have to leave their jobs, reduce their hours, or retire early. According to a poll of caregivers by Gallup, the majority of family caregivers report that their role has negatively impacted their career. Furthermore, the MetLife study mentioned above found that the average caregiver's lost wages are $143,000.

b. Decreased Employability. Caregivers who leave the workforce for months or years often find that it's difficult to get another job when their time as a caregiver ends. This challenge is particularly marked because high unemployment has created an extremely competitive labor market

c. Increased Health Care Costs. Caregiving is physically and mentally taxing. Gallup researchers found that caregivers have both worse physical and emotional health than non-caregivers. What's more, a study by the Center on Aging found that more than 1 in 10 caregivers say that the role has caused their own health to decline. This translates into increased healthcare costs for family

caregivers, particularly those who have lost their own health insurance because they left their job to become caregivers.

d. Lost Savings and Retirement. Out of pocket expenditures by caregivers can really add up. A study by the National Alliance for Caregiving and Evercare found that a stunning 47% of working caregivers reported having used up all or most of their savings. Naturally, caregivers who have left the workforce altogether will have an even more difficult time maintaining their savings and retirement funds. Leaving the workforce can also reduce your social security benefit.

e. Reduced Productivity. The costs of caregiving are not solely on the caregiver. The American economy itself is also impacted. MetLife found that American businesses lose an estimated $34 billion each year due to employees' need to care for aging loved ones

One reason that caregiving is so costly is that, according to MetLife, caregivers typically underestimate the amount time they will be providing care. We might imagine ourselves providing care a few hours per week for a couple of months, but end up providing care a few hours per day for a couple of years. Leaving the workforce for two months may be tolerable, but leaving the workforce for a couple years can be financially decimating.

THE ASSISTANCE COST.

1. Non-skilled (Companion/Personal Care) Assistance: the national average hourly fee for a home aide is $18 with different state averages ranging from $15 - $25 if hired through an Agency. In addition, agencies may charge cost differentials for care on weekends or holidays.
2. Certified Nursing Assistants (CNAs): a certified nursing aide is usually hired by the hour and can work for just several hours a day or week, or work full-time. The average hourly rate is $19. The typical pay range is $15-$30 an hour through an Agency.

EMOTIONAL CAREGIVER RELATED STRESS

With aged patients, the worse scenario is the "key closed patient", a way to precipitate quickly the loved health (mental and physical) condition.
The patients suffering from Alzheimer's have to be encouraged in activities and relationship with the community, under a various and expensive monitor.

Although the Alzheimer Association, Autism Association, Epilepsy Associations help caregivers in the management of the diseases, the caregivers generally suffer from emotional disorders due to less lifetime to spend with children, activities, work, less money to spend for enjoy and, finally, the fear of wandering/coming lost of patients or to be not promptly noticed of the need of the loved.

*A typical example.*
The Alzheimer's disease generally strains the family's finances. The management costs of the disease in the US is 180 billion USD (56,800 USD/ family/year, sources Alzheimer Association, http://www.alz.org/what-is-dementia.asp) (*MetLife says 38.000*)/y). Home health aides cost an average of $21 an hour, and assisted living facilities charge on average $38,000 a year: the money goes toward adult day care, nursing home, assisted living and paid caregivers such as companions and home health aides.

*A medical device, clinically tested, could allow caregivers to save money, suffering from less related stress and to improve the health condition of the loved, accordingly with the International*

*Scientific Community, the Scientific Literature, the Alzheimer's Association, the Autism Association and more.*

**THE PHYSISCIANS & THE DEVICE**

*Cardiologists can examine the patients heart by stethoscope, Electrocardiogram, BodyGuardian, like Holter exam, ultrasounds, and more (as TC-MR).*
*An heart damage is forever apparent.*
*Medical therapies and surgery improve the life quality and expectancy.*

*We know very few about neurological diseases and related behaviours.*
*All the outcomes of therapies, e.g. after discharge from Hospital, are completely transferred on patients themselves and/or their caregivers and to diaries they subjectively write on .*

*The CSP medical tracker device allow Physician to make differential diagnosis, promptly remote monitor a great variety of symptoms, adjust therapies, verify the outcomes of therapy plans or experimental medicines, monitor the trend of the disease.*

*Our medical tracker is intended for the clinical worldwide use in all the patients suffering from neurological diseases, and furthermore to prevent and care the typical behavioural changes in autism and epileptic seizures (see attached).*

All the intended use will be clinically tested.

## THE MARKET SCENARIO

The **Wall Street Journal**, Feb 16 , 2015 – by Jonathan D. Rockoff
*"Remote Patient Monitoring lets Doctors spot trouble early for patients with chronic conditions, tracking of vital signs allows quick adjustments in care"…*

The Senior Global and E-Health Advisor in the U.S. Department of Health and Human Services, in the past White House advisor on health issues, **Susan Blumenthal**:
*"Wearable devices are changing the way people interact with their own health. According to a report issued by the Health Research Institute, 21% of US consumers currently own a wearable technology product. As of June 2015, there were 196 medical or fitness related wearable devices on the market, with an average price of $310. Additionally, 71% of 16- 24 year olds report that they would like to have a smart band or Google Glass. According to another study, 68 million fitness trackers and health gadgets will be shipped to consumers this year. In 2014, 70 million of these devices were sold worldwide. There are over 140 million people living with at least one chronic medical condition in the United States. These individuals and their health care providers have a huge stake in monitoring their health - after all, the novelty of a product is less likely to wear off if you are using it to stay out of the hospital or to prevent a potentially lethal event! A recent survey found that 62% of people with chronic medical illnesses, including diabetes and heart disease, spent time every day tracking their health status while only 19% of those without a chronic illness did the same. An international group of more than 29,000 self-trackers is in its seventh year of efforts to convene users and makers of self-tracking tools. After last year's Wearables and Things conference in Washington, D.C., one physician called on techies to move away from the fitness arena alone and embrace medical applications as well. Only then can innovators bring their expertise to meet the needs of our nation's chronically ill and aging population who account for a large proportion of America's rising health care costs. Some technology companies have risen to the challenge with new products. Patient-consumers can purchase headsets that measure brain activity, chest bands for cardiac monitoring, motion sensors for seniors living alone, remote glucose monitors for diabetes patients, and smart diapers to detect urinary tract infections. Based on data from electronic sensors that track internal body temperature, another innovation sends female users a text message when it's their optimal time to conceive a baby. A large tech company's research arm is pilot testing an anti-shake spoon to counteract the tremors caused by Parkinson's disease and is working with another company to develop glucose-measuring contact lenses for patients with diabetes. Currently, you can monitor hypertension with a blood pressure cuff or your glucose levels with a finger prick. But in the future, smart phones and other connected devices might do this automatically, alerting you, your family, and your doctor if there are significant changes if you are sick. New technologies are even being developed that will measure bodily changes from the inside out - using chips that are ingestible or float in the bloodstream. And IBM is training its Watson computer to be a cancer specialist at the MD Anderson Cancer Center.*
*Remote patient monitoring merges wireless technology and medical care focusing on serious, chronic conditions like heart disease and diabetes. Some hospitals and clinics are installing routers in patient homes to collect continuous data on weight, blood pressure, glucose, and blood oxygen levels. Physicians can then make quick adjustments to care without having to bring their patients in for an expensive medical visit. These integrated systems also allow health care providers to detect issues before they have serious health consequences".*

SEE ALSO:

http://www.startuphealth.com/video/index/49548?utm_source=StartUp+Health+Insider&utm_campaign=857d24ef5a-StartUp_Health_Weekly_News_07-13-2016&utm_medium=email&utm_term=0_250bac26a5-857d24ef5a-312351509

## THE STATE OF THE ART

In US there are 56 medical devices on Market (http://vandrico.com/wearables).
No one has the features of ours.

In the complete lack of medical devices for neurological diseases, the existing are intended only to perform few functions, as the "geo localization" of patients suffering from Dementia.
They are generally mobile phones transformed and adapted to various "trackers".

***Alzheimer's.***

*The Alzheimer's Association suggests devices derived from cell phone with GPS module. They are expensive, require frequent battery charging, are not medical devices, are not clinically tested, are lack of specific algorithms, do not allow a geo fencing; the localization is on request and costs about 50 USD/month for a response within 30 minutes to 65 USD/month to reply within 15 minutes of calling the caregiver.*

More solutions (http://www.alz.org)

Confort Zone™ (http://www.alz.org/comfortzone/about_comfort_zone.asp)

**Comfort Zone™** is a Web application that includes a *location-based mapping service, or LBS* . This term refers to a wide range of services that provide information about a person's (or object's) location. If you've ever used a GPS device in your car for turn-by-turn driving directions or tracked a package online, you've used LBS.
Here's how LBS works with Comfort Zone: A person with Alzheimer's wears or carries a locator device (such as a pager or wrist-worn device) or mounts one in his or her car. As the person travels around town or the country, the device receives signals from satellites or nearby cell towers. The device can then approximate the person's location by measuring the distance between the device and the cell towers or satellite signals. The device communicates with the Comfort Zone Web application. Family members access information about the person's location by using the Internet or calling the monitoring center.
Families can also decide on the level of monitoring needed, such as verifying location from a computer; receiving alerts when the person has traveled in or out of a zone; or just emergency assistance if there is a wandering incident.
Comfort Zone is a full service application, offering you an easy to use and secure Web monitoring site plus access to 24/7 live support and the resources of the Alzheimer's Association.
**Comfort Zone plans start at $42.99 per month plus a $45 activation fee.** A Comfort Zone plan is designed specifically to each device.
**Web application features include:**
Scheduled day and night zones; Additional trip zone, to set up another zone when vacationing or visiting another location; Zone exit and enter alerts; Find Me current locates, to see a person's location on a map; Follow Me constant tracking, to follow a person's movements on a map for a 60-minute session; Alerts via text, e-mai; Location history; Privacy management.
**Plus these additional services:** Emergency medical health record by MedicAlert Foundation; 24/7 emergency response; 24/7 location assistance; 24/7 care consultation; Application support; mMedicAlert® + Alzheimer's Association Safe Return® bracelet;m Alzheimer's Association resources.
**Supports device-dependent features**: Panic, voice, fall detection, reminder services. Type of communication method between Comfort Zone and the device influences monthly plan fee.


**MedicAlert® + Alzheimer's Association Safe Return® is a 24-hour nationwide emergency response service** for individuals with Alzheimer's or a related dementia who wander or have a medical emergency. We provide 24-hour assistance, no matter when or where the person is reported missing.
MedicAlert + Safe Return provide an ID bracelet or pendant to be worn by the individual with dementia.
**$55 + $7 shipping and handling, you receive an enrollment package including:** Member's ID jewelry with personalized information and MedicAlert + Safe Return's 24-hour emergency toll-free number; Personalized emergency wallet card; 24-hour emergency response service; Personal health record (PHR); *Six Steps to a Safe Return* magnet
**(Optional) Add $35 for caregiver ID jewelry and membership**; Membership includes everything listed above; The caregiver wears this worldwide-recognized ID jewelry to alert others that he or she provides care for a MedicAlert + Safe Return member, in case of an emergency.

**MedicAlert® + Alzheimer's Association Safe Return® is a 24-hour nationwide emergency response service** for individuals with Alzheimer's or a related dementia who wander or have a medical emergency. We provide 24-hour assistance, no matter when or where the person is reported missing.
MedicAlert + Safe Return provide an ID bracelet or pendant to be worn by the individual with dementia.
**$55 + $7 shipping and handling, you receive an enrollment package including:** Member's ID jewelry with personalized information and MedicAlert + Safe Return's 24-hour emergency toll-free number; Personalized emergency wallet card; 24-hour emergency response service; Personal health record (PHR); *Six Steps to a Safe Return* magnet
**(Optional) Add $35 for caregiver ID jewelry and membership**; Membership includes everything listed above; The caregiver wears this worldwide-recognized ID jewelry to alert others that he or she provides care for a MedicAlert + Safe Return member, in case of an emergency.
**$35 annual renewal fee**. An annual fee of $35 will be due after the first year for each membership.

## CalAmp LMU-2610 Vehicle Tracker™

**http://www.alz.org/comfortzone/downloads/CZCalAmp2610InfoSheet.pdf**


CalAmp, sold by Omnilink; System: GPS. Type: Car, requires professional installation. Network: AT&T via Jasper Wireless. Comfort Zone Allowance Includes: Monthly Location monthly allowance: 30 Comfort Zone Find Me Locates (current location); 2 Comfort Zone Follow Me Sessions (constant tracking). Overage Allowance Costs: $ .10 per Comfort Zone Find Me Locates (current location); $ 5.00 per Comfort Zone Follow Me Session (constant tracking)

## Keruve ™ *Price from 850 to 1.499 USD. Battery life 3 days. No fence*


Keruve gives your family member with Alzheimer's the ability to continue going for walks as usual without having to worry about them getting lost. With the press of a button you can quickly know where they are at any given moment. Specifically designed for people in the first stages of Alzheimer's, Keruve is a state of the art locating device that consists of a GPS wristwatch with safety lock, worn by the person with Alzheimer's, and a portable receiver for the carer.
By simply pressing a button on the receiver you can locate the person and a map will appear on the screen showing their exact position. Locate them without intermediaries, with no distance limits, anywhere, quickly and effectively.Our only aim is to improve the quality of life for people with Alzheimer's and their families. Collaborating with the most important Alzheimer's associations and listening to our thousands of customers in over 20 countries, has enabled us to know what is needed to have peace of mind and trust every day.

## *Sleep Disturbance*

The most common exam for overnight sleep monitoring, considered as gold standard, is the ***polysomnography*** (PSG), usually performed at night into an Hospital. The PSG can monitor many body functions including brain (EEG), eye movements (EOG), muscle activity or skeletal muscle activation (EMG) and heart rhythm (ECG) during sleep, and breathing functions respiratory airflow and respiratory effort indicators with peripheral pulse oximetry. Technical Fee - $3500.00. Physician Fee - $1100.00

***Actigraphy*** (see e.g. www.actigraphy.respironics.com/applictions/clinical_sleep.html - PHILIPS™) is generally a three axis device for monitoring human rest/activity cycles. A small actigraph unit, also called an actimetry sensor, is worn for few days week to measure gross motor activity. The unit is usually, in a wrist-watch-like package, worn on the wrist. The movements the actigraph unit undergoes are continually recorded and some units also measure light exposure. The data are typically analyzed offline.

**Home Sleep test** (HST). Users usually go into a Sleep Clinic the day of the test to pick up their HST and are given a demonstration on how to use the machine properly before taking the equipment home. The data stored is uploaded the following day at the sleep clinic. Technical Fee - $800.00 Physician Fee - $500.00
http://www.alaskasleep.com/blog/costs-sleep-studies-rates-fees-discounts

**CPAP Titration Study** usually follows a PSG diagnostics test. It involves much of the same equipment used in a PSG but also includes sleeping while using a CPAP machine and mask to see how the patient's body responds to the therapy. Technical Fee - $4000.00. Physician Fee - $1200.00

**Multiple Sleep Latency Test** (MSLT) is a sleep study that is performed during the day to measure how sleepy you get or to discern whether breathing treatments for your disorder are working properly. MSLT's generally follow a Polysomnogram and record whether you fall asleep during the test, and if so, which stages of sleep you enter.
Technical Fee - $2500.00; Physician Fee - 1200.00

**Maintenance of Wakefulness test (MWT)** is a daytime sleep study that measures how alert users are during the day and their ability to stay awake. Usually performed after a PSG, can help determine if the sleepiness is a safety concern. In a MWT the patient lays on a bed in a dimly lit room while trying to stay awake 4 times at 20 minute intervals spaced 2 hours apart. Results of an MWT can be critical if a person's job involves public transportation. Often, employers will require an employee to have an MWT if they have a history of excessive daytime sleepiness or other related sleep disorders. Technical Fee - $2500.00; Physician Fee - $1200.00

***Empatica*** www.empatica.com https://blog.empatica.com/introducing-the-embrace-clinical-trial/


*"We develop groundbreaking wearable devices with clinical quality sensing. We are a super passionate team, from diverse engineering fields, such as sensor design, electrical, DSP, data science, biomedical, and software development and wearable.*
*We design and develop the world's smallest and most accurate wearable device for medical research of human behavior in daily life. Our E4 is used in 30 countries around the world, its clients are the most respected hospitals, universities, and companies that use it for advanced research on human behavior. The E4 provides the most sophisticated way to monitor autonomic nervous system disruption and heart rate variability, among a set of 5 sensors.*
*We are launching the Embrace watch, a wearable device designed to save lives, that has just completed a very successful crowdfunding campaign."*

*Cost: from 199 USD plus service – unknown - till 1690 USD*

The most advanced device ready for the Market is Empatica.
The differences vs our device are great: it needs a gateway (smartphone, dedicated if medical device), and it is lacking of modem, GPS, magnetometer, algorithms, is not water proof, not shockproof. It uses plethismography and electrodermal sensors for ecg and more, and the scientific Community generally doesn't like these measurements because are not accurate.

Deeping undergoing, the devices today on Market for Alzheimer's have several limits: high average cost of the device and average cost of service, difficulty of management by the patient and family, often lack alarm (alert) for trespassing the virtual fence (geofancing), often need to call an Operating Room Centre for the coordinates of the Patient, size and weight, not waterproof, not shock proof, very basic algorithms, lack of scientific validation, battery life.

The *battery life* is the weak point of the devices on the market today. By definition, a patient suffering from dementia can not remember things. So can not remember to charge the battery of the device. The average battery life of the devices on the market varies from a few hours to a few days, and this depends mainly on the physical characteristics (size, power, and energy used by the device, this is directly proportional to the amount of data downloaded by the same).

We have therefore designed a device that meets these requirements (see attached technical features):

1. Safety
2. Specific and dedicated algorithms
3. Easy use
4. Long last battery life
5. Low cost of ownership
6. Clinical and scientific validation

*The first kind of device we designed and projected was innovative because characterized by the following requirements:*

a) extremely easy to use: when you register your product (coupled SIM/user/billing information) on the portal of CSP, the device is immediately operative, easy to use and extremely intuitive

b) a wearable beacon defines the fence, out of it the GPS signals the position.

c) algorithms allow employees to acquire data on the habits of life of the subject, for example if you usually moves quickly or less, and to report the stepped change in lifestyle

d) the device is small, wearable, shock resistant, waterproof bracelet

e) considerable saving of battery. The charge level of the battery is monitored by CSP, and we send to the known address a new device to replace the previous

f) signal trespassing (alert) is sent automatically and instantly to the family or caregiver via SMS (or phone call depending from the alert), the more frequently the more the subject moves away from the virtual fence. Even a change in lifestyle habits (increased walking speed or its opposite, motor agitation, prolonged immobility) is reported. The data set in the factory can be modified by the caregiver in case of need, by accessing the portal CSP. If the patient moves to the doctor, ig, the family can disable the alerts by accessing the portal CSP, or disabling the same through a special app on your smartphone,

g) the geo localization is easily displayed on smartphone or pad or PC via the CSP server. The same has always possible if the subject is outside the virtual fence. In case of power failure at home (or detachment Power Plug HUB home) the family or the caregiver is alerted through specific message; the device transmits the position of the subject at regular intervals

h) the device is tested at the Carlo Besta Neurological Institute, the European Centre of Excellence for Alzheimer's, Parkinson's, Sleep Disturbance. We expect a good number of publications in qualified international scientific journals.

i) the form of transmission via GSM SIM makes the data inaccessible to third parties other than the judiciary or entities specifically authorized (clinics, hospitals, and so on prior authorization).

## THE ALGORITHMS

*Specific and dedicated ALGORITHMS allow the device to monitor the habits and check the movements of patients during the daily life.*
*At now is not possible to monitor movement impairment and/or neurological Syndromes and/or have objective outcome e.g. of efficacy of therapies.*

*We translate the signals from the device in clinical evidence, understanding when, how, why, and easing a differential diagnosis.*

*The dedicated and of high complexity architecture allow us to receive synchronized input from the device to be translated into use cases or "clinical classifications" and consequent different actions.*

1. Geofencing via beacon
2. Fall Down
3. Myoclonic movement
4. Fasciculation
5. Dyskinesia
6. Pill rolling
7. Resting tremor
8. Muscle stiffness
9. Postural instability
10. Balance instability
11. Freezing
12. Impaired coordination leg-arm
13. Speed of arm movement
14. Speed of motion (walking)
15. Fluidity of movement
16. Degree of difficulty of movement
17. Degree of difficulty in getting up (with number of attempts)
18. Amount of hours lived in bed or on a chair
19. Wandering (Alzheimer's – Autism)
20. Elopement (Alzheimer's – Autism)
21. Running (Autism)
22. Rocking body (Autism)
23. Spinning in circle (Autism)
24. Hyperactivity
25. Idleness
26. Sleep disturbances
    a. Insomnia (*with BG*)
    b. Somnambulism (*with BG*)
    c. Sleep Apnea *(with BG-oximetr)*
    d. Restless Leg Syndrome (*with or without BG*)
27. Seizure (Epilepsy)
    a. Kind
    b. Where
    c. When
    d. Wave (Hz) of seizure
    e. How long

28. Seizure with consequent fall down
29. Fall down consequent with seizure
30. Spasm (Corea) and other muscle diseases (a,b,c,d…)
31. Validation of therapies
    a. Parkinson
    b. Epilepsy
    c. Autism
    d. Sleep disturbances
    e. Unusual habits
    f. More
32. Validation of new therapies compared with past therapies
33. Trend of the disease
34. Outcome of clinical trials or therapies
35. Paired with BodyGuardian: monitoring of acetylcholine therapy and related syncope
36. Behavioral control and Therapy in Autism: active sound Therapy.

Every clinical issue is delivered to the server and here it is processed and classified with score 1….5.
We assign an alert (0 to 10) with a "Bonus Theory" of classification (e.g. 0,+1,-1) from the basis of the first day, and from here on the average of all the past days.
The event could be single or recurrent (1 to 3).
The seriousness is classified from 0 to 3.
The match of one ore more alerts produces a code of alert (0…. to many thousand, as different clinical combination) to be translated on the platform in CLINICAL EVENT.
See "SERVICE".

Please, note:

1. The "Saving energy for emergencies function" (Alzheimer's and Autism) allows to track the patient with the possible less consumption of battery since "last signal" of the known position before turning off of the device itself.

2. We can inform directly the Patient or caregiver with a short message on the display, e.g. remind of "pill assumption" or "charge battery" or "call the doctor".

3. It is available a call from and to the Patient through the "Emergency button".

4. A short clinical report could be transferred via BT to a smartphone of The Emergency Team after the OK of the Operating Room

## THE SERVICE

*The device's use is very easy: "wear it, and forget it".*

(The Patient and/or the caregiver has to remember only to charge the device when necessary).

After registration on our portal, the device is enabled for the related monitoring disease.
We designed three levels:

1. Patients and caregivers can adjust themselves messages as reminder for appointments or therapies. Caregivers can see everywhere and every time where is the loved and if he or she is well.
2. Physician. The Doctor can adjust the parameters and the threshold, reminder therapies and clinical control. He sees on the portal all the clinical elaborated and classified data as events, graphics and status messages.
3. Administrator. All the functions.

The Service we supply on server HIPAA compliant is completely automatized, 24/7 e.g. for messages of status, battery level, pills reminder and more.
All the events received from the device are recorded on the Patient History file.

The Operating Room is available 24/7 via the SOS button.

The Patients or the Caregiver pay the service through a credit card. We established an advance monthly fee for the Service (from 20-25 USD/month for Alzheimer's up to > 40 USD/month for Parkinson's according with the functions "on board" and the intended use) plus SIM traffic and calls from the Operating Room if needed.

*We trust a little price promotes the approval of the Market and it is economically and politically correct to support families.*

When the CLINICAL EVENTS arrive to the server, the related code allows four different chooses:

1. Minor event. The event is recorded.

2. Middle event. The server sends different messages, related to different events, to the smartphone of the caregiver or Physician or Hospital for possible middle events to be monitored personally.

3. Major Event: the server informs promptly the Operative Room in TeSAN, a TBS Group, to call the caregivers or phone numbers registered for possible Major Event that needs qualified assistance.

4. The Operation Room can call 24/7 Emergency Numbers (in Italy 118, in US 911 and so on) knowing the last position of the patient.

Any time, everywhere is 3-4G or LTE or Wi-Fi signal, caregivers can see where is the Patient on a PC (on our portal) or directly on own smartphone, define a virtual fence, call the patient.

A free App (IOS Apple or GooglePlay) is available.

## OUR CLINICAL STUDIES

*We trust strongly it is necessary to run to the Market through a rigorous clinical test.*
*We want people know the device thanks to:*

1. Clinical World
    a. Neurologists
    b. Hospitals
    c. Doctor's offices
    d. Medical Congresses
    e. International scientific publication, with the highest impact factor we warrant to them thanks to our disruptive device and the opportunity, for the first time, of a remote monitoring of neurological diseases and related behavior
2. Alzheimer's, Parkinson's, Autism, Epilepsy Associations network, everywhere.
3. Media

*And we want every Neurologist will recommend to his patient the CSP medical device because it is simply essential for the Physician himself (better care, monitoring and so on) and for the Patient.*

For achieve this target, we thought to design and execute clinical trials with the greatest and famous Clinical and University Hospitals in Milan, as:
**Carlo Besta Neurological Institute** (www.istituto-besta.it), the most famous Hospital for neurological disease in Italy and very named in Europe, like Mayo Clinic in in the US for cardiovascular disease. The Carlo Besta Hospital depends directly from Ministry of Health and is the national Center e.g. for Alzheimer's. Clinical trials:

1. Alzheimer's. To enrich this kind of difficult clinical Protocol, we engaged the "Mario Negri Institute for Pharmacological Research" (http://www.marionegri.it), everywhere famous.
2. Parkinson's
3. MCI
4. Sleep disturbances
5. Epileptic seizures into Hospital (before and after surgery and after ictus)
6. Fall Down into Hospital
7. Stroke: to be designed
8. Rehabilitation: to be designed

**San Paolo Hospital,** in Milan (http://www.ao-sanpaolo.it), a very famous University Hospital depending from Ministry with the largest Italian experience and on children focused experience in:

1. Autism in children
2. Epilepsy in children
3. A model of new therapy. The autism, & the noise: from the adverse event to the active noise control

We are currently working with the Italian Alzheimer's Association, the Parkinson's Association, and we want to engage the Michael J fox Foundation, the Epileptic Association, the Sleep Association, the NeuroSurgery Association and so on.
We can take a lot of advantages from international GRANT from Horizon 2020, MJFF, Autism Society, Suzanne and Bob Wright Trailblazer Award Program etc.

MORE OPPORTUNITIES.

A nice not-clinical Market opportunity is to offer the device for parents who want check the daily activities of own children e.g. on the beach or during excursions.

## GOING TO THE MARKET

It will be possible to buy the device on the Market at Pharmacies, as prescribed from Physicians or recommended from the Associations; the CE medical I device is saleable by TelCo.

A small and lightweight rigid box will contains the device, the beacon, brochure, charging pad and more items.

*The device is the same for all the intended uses.*

Accessing to our CSP portal, it is very simple to register information (PW – ID - "I'm not a Robot" and so on), to couple and to synchronize the device and to choose the intended use.

The specific software is then transcribed on the device, so prompt for the intended use.

## REIMBURSEMENT

Many functions of our medical device are yet directly reimbursed as the at Hospital exams e.g. for sleep disturbances. We are greatly competitive, because our solution allows at home exam and the devices are not so expensive.

The Insurances (typically in US and North Europe) and the Ministry of Health could reimburse directly the costs for the medical device and related service for the intended use in Hospital or at home.

The saving money is determined by:
-long remote monitoring period with trend evaluation
-prompt alert about health conditions (epileptic seizure, fall down, somnambulism and so on)
-better therapy
-better quality life
-supporting caregivers' activity.

## SYNERGIES

Our medical tracker device is intended to control-avoid elopement-going lost of Alzheimer's and Autism, confirm clinical outcomes, collect clinical data, evaluate the trend of disease, care/prevent behavioral changes or epileptic seizures.

This allows synergies with:

*Pharmaceutical Industries.*

a. Parkinson's. Pharma are always studying medicines and clinical protocol to care of people suffering from Parkinson's.
b. Sleep disturbances. The MTD allows to evaluate finely the sleep disorders and the daily-night time activity, suggesting the right therapy and right timing and dose of medicines. Furthermore, many people suffering from Parkinson's has sleep disorders.
c. Epilepsy. The MTD allows to validate the right dose of medicines and study new chemical.

d. Interaction between acetylcholine assumption and syncope

2. *Insurances*.
   a. They need data to evaluate the trend of diseases and assess balanced insurance premiums in people suffering from neurological diseases.
   b. Workers with Sleep Disorders could have or produce accidents

3. *Companies*.
   a. Direct-indirect interest in the building the MTD
   b. Using the MTD as gateway replacing the smartphones (expensive, non water and shockproof, often complicated to use for oldest people)
   c. Building new diagnostic models as for the sleep disorders opening growing markets
   d. Interaction with products as GONDOLA® for Parkinson's, confirming their utility and trend/improvement of disease

4. *Associations - Foundations.*
   They are worldwide interested to suggest devices helping people suffering from neurological disease.
   a. Alzheimer's Association
   b. Michael J. Fox Foundation
   c. Parkinson's Associations & Foundation
   d. Epilepsy Associations & Foundation
   e. Autism Associations & Foundation
   f. Sleep Disorders Associations & Foundation
   g. Care Giver Associations
   h. Stroke Associations
   i. Neurological Associations
   j. More

**GRANT**

Many Associations and Foundation, as privates, supply funds for clinical and chemical Research, supporting Clinical Trials and confirming their outcome.

Clinical Trial as the MCI one (300 patients for 3-5 years) could be performed supported from international grants as Horizon 2020.

*Marcello Ruspi, Ph*
*Vascular Surgeon*
*Founder and Medical Chief*
*CSP Telemedicine S.r.l. Care Save Prevent*
*Milan - Italy*

*On intended use invention and elaborating, planning, projecting, designing clinical trials and algorithms ideation, project and elaboration IP applied.*

*Milan, November 18th 2015*