SONoALS

Early diagnosis and Acceleration of drug discovery for ALS

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The Problem

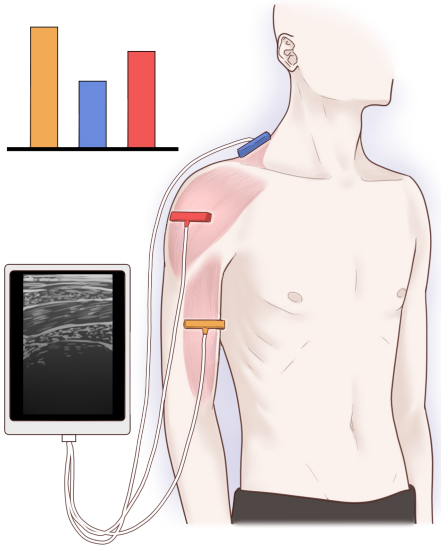
ALS is a progressive neurodegenerative disease that causes the degeneration and loss of motor neurons, leading to generalized muscle weakness and atrophy. Most patients experience respiratory failure and either death or transition to mechanical ventilation within 2–5 years of onset.
While ALS appears rare with a prevalence of just 5 per 100,000 people, the **lifetime risk of developing ALS is surprisingly high—affecting 1 in every 300 individuals**. This discrepancy highlights a harsh reality: the low prevalence reflects not rarity, but the **short survival period** after diagnosis.
Although recent years have seen the emergence of treatments that modestly slow disease progression, there is still **no definitive or curative therapy**. It has become clear that, for some new drugs, early initiation of treatment is important. **Early diagnosis and early intervention are critical**, and there remains an urgent need for breakthroughs in **curative therapies.**

The Solution

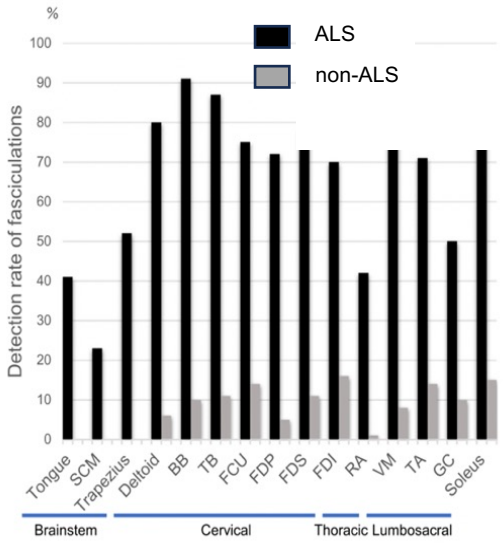
We propose a non-invasive, early diagnostic and therapeutic biomarker platform for ALS by combining:

- A **wearable ultrasound device** capable of simultaneously monitoring **up to 12 muscle sites**, and
- AI-based detection and quantification of **fasciculations**—the hallmark of lower motor neuron signs in ALS.

Unlike traditional ultrasound techniques that are limited to brief snapshots (typically less than 60 seconds), our approach enables **continuous monitoring for 20 to 30 minutes**, allowing for **quantitative assessment** of fasciculations for the first time.
This significantly enhances the potential to replace **invasive needle electromyogram (EMG)** with a **painless, user-friendly alternative** for early ALS screening.
Moreover, we aim to establish clinical evidence supporting its use as a **treatment response biomarker**, enabling rapid evaluation of drug efficacy in clinical trials and personalized therapy.

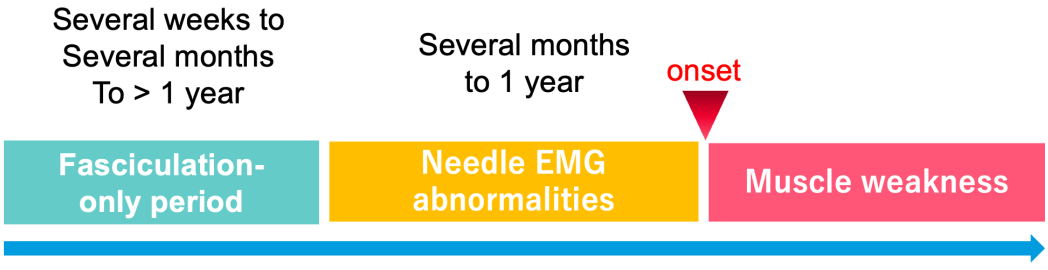


1-1. As an Early Diagnostic Tool
— Technology —
A previous study from Tokushima University (Fukushima, 2022) demonstrated that conventional handheld ultrasound can detect fasciculations in 8 muscle sites with **90% sensitivity and 92% specificity** for early ALS diagnosis.
Building on this, our wearable ultrasound device combined with AI enables **automated detection** of fasciculation frequency and distribution across selected muscles.
Certain muscles exhibit fasciculations with high disease specificity, and leveraging this pattern allows for **even higher diagnostic accuracy**.
The test is extremely simple and patient-friendly:
By attaching wearable ultrasound patches to multiple muscles and having the patient lie still for 20 minutes, the system autonomously records and analyzes fasciculation activity—offering a non-invasive, highly sensitive tool for early ALS diagnosis.



(*Fukushima et al*, 2022)

1-2. As an Early Diagnostic Tool — *Significance*
Fasciculations (muscle twitches) are among the earliest observable signs of ALS, as shown below. In Japan, it currently takes an average of **13 months from onset of muscle weakness to a confirmed diagnosis**—a significant diagnostic delay.
However, recent therapeutics like Rozebalamin have demonstrated **clinical efficacy only when initiated within the first year after onset**, with stronger effects observed the earlier treatment begins.
This underscores an urgent need for **early diagnosis and intervention**.
Our device can detect fasciculations non-invasively and objectively in the earliest phase of ALS, offering patients and clinicians a **critical window of opportunity** to begin treatment when it is most effective.
This diagnostic innovation holds substantial clinical and social value for ALS patients.



1-3. As an Early Diagnostic Tool – Market Opportunity

Needle electromyography (EMG), which is invasive and painful, is currently the standard diagnostic method for ALS. By lowering this barrier, our device provides earlier and more accessible testing opportunities—not only for the 400,000 ALS patients worldwide, but potentially for healthy individuals as well.

In fact, surveys show that up to 70% of healthy people experience fasciculations (muscle twitching). When people search terms like “muscle twitching” online, “ALS” is often among the top suggested results. While most of these twitches are benign or physiological, many individuals are left anxious, unable to access testing due to the invasive nature of current diagnostics.

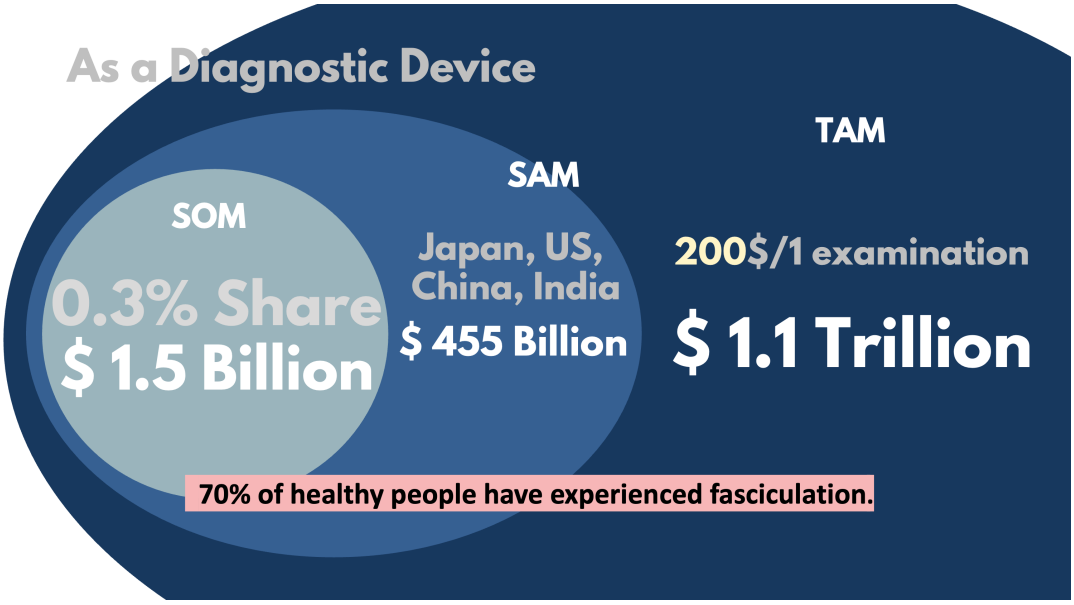
We envision a world where early screening for neuromuscular diseases can be easily performed at health screening centers, clinics, home visits, hospitals, or even at home. Being able to confidently diagnose someone as *not* having ALS is equally meaningful.

In the near future, a combination of our device and blood-based biomarkers may become the new standard for presymptomatic screening of rare neurological diseases.

Market Opportunity and Global Strategy

Assuming a price of $200 per test, even capturing just 0.3% of the addressable market across Japan, the United States, the European Union, and China—our target regions for patent registration and regulatory approval—would result in projected revenues of approximately **$1.5 billion**.

We will launch a domestic clinical study in FY2025 to validate the diagnostic accuracy of our device through ROC curve analysis, sensitivity, and specificity. In FY2026, we plan to initiate regulatory preparation for clinical trials in **Australia**, followed by a pathway toward **FDA approval** in the United States. Ultimately, we aim to secure **PMDA approval** in Japan.



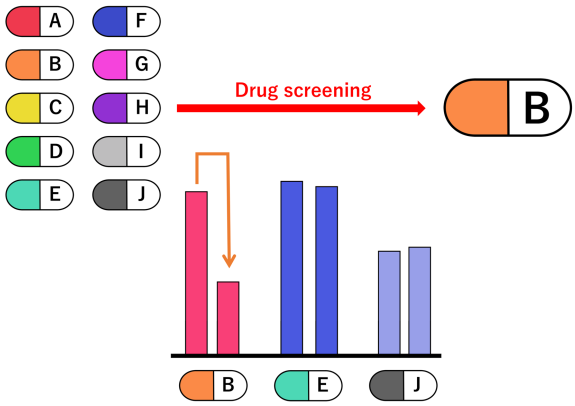
2. As a Tool for Evaluating Drug Efficacy

Beyond early diagnosis, the primary application of this technology is to **rapidly assess the therapeutic efficacy of drug candidates**.

2-1. Pre-Trial Human Short-Term Drug Screening

Before launching full-scale clinical trials, this device enables short-term screening in humans by monitoring fasciculation frequency. If fasciculations significantly decrease within 3–7 days after a test dose of an investigational drug, the compound is likely to be effective. (We plan to validate this approach through clinical studies.)

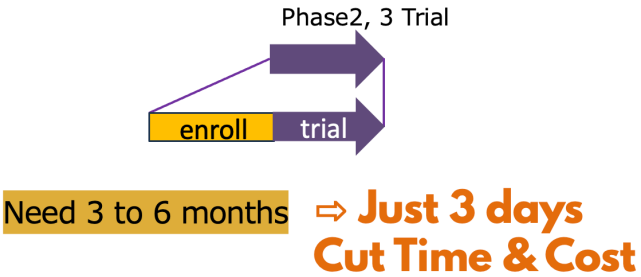
This process allows sponsors to prioritize promising compounds for full trials, helping avoid the common pitfall where drugs that show efficacy in iPS cell or animal models fail to demonstrate effect in humans. Early-phase human screening is crucial for improving the success rate of ALS trials.



2-2. Reducing Screening Periods in ALS Clinical Trials

In Phase 2 and Phase 3 clinical trials for ALS, patients typically undergo a 3–6 month observation period before being enrolled. During this time, they receive no investigational treatment while their disease progression is monitored — mainly to exclude those who progress too quickly or too slowly based on functional rating scores. Considering ALS patients face an average life expectancy of only 2–5 years, this delay is ethically and emotionally challenging.

Our device offers a solution: by administering a test dose of the investigational drug for a few days and observing a meaningful reduction in fasciculation frequency, eligible patients can be identified rapidly. This approach could serve as a novel and humane alternative to prolonged screening, accelerating enrollment while preserving ethical integrity.

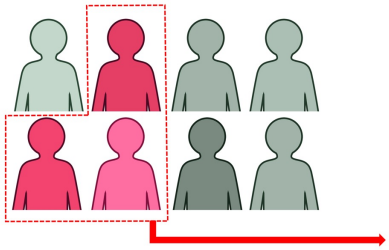


2-3. Identifying Potential Responders for Clinical Trials

Even the most promising drug can fail in a clinical trial if, by chance, the enrolled participants are predominantly non-responders—patients who do not respond to treatment. This is a critical risk in ALS drug development.

Our device enables the identification of treatment responders within a few days by detecting significant reductions in fasciculation frequency following trial dosing. However, directly selecting responders for enrollment may compromise trial design and regulatory approval.

Instead, our device can be used to extract characteristic features of responders. These features can then inform inclusion criteria for clinical trials, ensuring that a higher proportion of likely responders are enrolled—significantly increasing the probability of trial success.



No more wasted time or patients' lives.

2-4. Therapeutic Efficacy Evaluation Device – Business Strategy

Our primary objective is to support clinical trials and drug development by enabling pharmaceutical companies and clinical investigators to generate success stories using our device. By demonstrating treatment efficacy more efficiently, we aim to accelerate the path to new therapies.

Our target customers include pharmaceutical companies and principal investigators at medical institutions. The goal is widespread adoption of the device in research settings across the globe.

3. Timeline and Mission

For early diagnosis, our aim is to widely disseminate this device as a screening tool, with a business model that generates most of its profit from healthy individuals. This allows us to offer the device to ALS patients at a more affordable price point.

The development timeline is illustrated below. Using research grants already secured, we will conduct a feasibility study over one year starting in FY2025. Following publication of the results, we plan to release the device in the Japanese market as a non-insurance, private-pay medical service—prior to regulatory approval—at a fair and accessible price (targeting late FY2026 or FY2027).

Concurrently, we plan to begin clinical trials in Australia in collaboration with A/Professor Tina Soulis in FY2026, with the ultimate goal of gaining FDA approval, followed by PMDA approval in Japan, to enable insurance reimbursement. This approval pathway is targeted for completion within six years.

As for the therapeutic efficacy evaluation device, we plan to begin a three-year clinical study as soon as research funding is secured. Once the findings are published, the device will be offered to pharmaceutical companies and research hospitals as a research-use-only device to accelerate drug trials and facilitate the development of successful therapeutics.