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Why a Clinical Decision Support System is needed for Tinnitus?

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***Abstract*— Tinnitus is the perception of a phantom sound and the individual's reaction to it. Although much progress has been made, tinnitus remains an unresolved scientific and clinical issue, affecting more than 10% of the general population and having a high prevalence and socioeconomic burden. Clinical decision support systems (CDSS) are used to assist clinicians in their complex decision-making processes, having been proved that they improve healthcare delivery. In this paper, we present a CDSS for tinnitus, attempting to address the question which treatment approach is optimal for a particular patient based on specific parameters. The CDSS will be developed in the context of the EU-funded "UNITI" project and, after the project completion, it will be able to determine the suitability and expected attachment of a particular patient to a list of available clinical interventions, utilizing predictive and classification machine learning models.**

***Clinical Relevance*— The proposed clinically utilizable CDSS will be able to suggest the optimal treatment strategy for the tinnitus patient based on a set of heterogeneous data.**

I. Introduction

A. Tinnitus

Tinnitus is the perception of sound when no corresponding external auditory stimulus is present. This heterogeneous disorder causes significant impairment in many patients, as it is highly prevalent, affecting about 10-15% of the general population [1] and up to 25% of people aged over 70 years [2].

Tinnitus can be attributable to hearing loss, somatosensory system dysfunction, or auditory cortex dysfunction, with hearing loss being the most common cause and other serious underlying pathologies being rare [3]. However, hearing loss does not always lead to tinnitus, and patients with tinnitus do not always suffer from hearing loss. Also, tinnitus is often correlated with noise exposure, aging, and stress, but less often with other otologic, neurologic, infectious, and drug-related symptoms, as well as other comorbidities.

Comorbidities can be pre-existing or brought about by tinnitus. Tinnitus is often correlated with psychological, psychosomatic, and/or psychiatric comorbidities. Tinnitus patients also experience anxiety, depression, and insomnia. The greater the level of distress, the more definitely the presence of comorbid disorders [4].

Tinnitus can manifest itself in a variety of ways and proves to be a highly complex condition with a multifactorial etiology and, as a result, a wide range of patient profiles. During tinnitus assessment, physicians should determine any possible tinnitus-related causes. Nevertheless, tinnitus is not directly related to any medical condition in the majority of people. Standard treatment, evaluation, and referral pathways are ill-defined, ill-established, and often inadequate. Thus, the lack of standard protocols is likely to result in untreated, under-treated, and over-treated patients [5], [6], [7]. Also, given the complexity and heterogeneity of tinnitus, single factor strategies are likely to fail.

The crucial problem in the management of tinnitus is the fact that there is currently no cure available. The obtainable treatments options include hearing aids, wide-band sound therapy, structured counselling, and cognitive behavioral therapy, aiming at symptomatic relief and management of associated distress [8]. Other less commonly-used treatment options include surgical intervention and pharmacotherapy (e.g., lidocaine). Despite the apparently large variety of treatment options, the low success rates of tinnitus therapies lead to frustration of physicians and patients alike. For some specific patient groups (e.g., people with subjective chronic tinnitus) in particular, effective therapeutic options with guidelines about key diagnostic criteria are urgently needed. In this context, tinnitus should be treated based on an assessment that accounts for it as part of a complex system with intricate interactions between its constituent factors [9].

Although tinnitus is a common clinical condition with enormous prevalence and socioeconomic burden [10], it remains indeed a research and clinical mystery. It can have a detrimental effect on the afflicted person in a variety of aspects in their everyday life. It can occur at any age, with varying frequencies, intensity, and duration scales, and the annoyance caused to patients ranges from completely absent to tinnitus-related suicidal ideation.

Taking all these points into consideration, there is a need of more standardization in tinnitus research and treatment. The standardization is essential in clinical management of tinnitus patients, assessment methods, and outcome measurements, taking into consideration the heterogeneity of tinnitus. This will contribute in evaluating the performance of clinical trials, comparing the results across centers, conducting clinic audits, and performing epidemiological studies in the most efficient way [11].

B. Clinical Decision Support Systems

A clinical decision support system (CDSS) is a health information technology system that is developed to provide health professionals support with clinical decision-making

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process. CDSS can greatly assist in identifying diseases, facilitating diagnosis and methods of treatment, and minimizing the errors in medication prescribing [12]. Over the past years, CDSSs have dramatically improved their performance by deploying artificial intelligent algorithms, paving the way for precision medicine [13]. CDSSs represent a paradigm shift in healthcare today and they actively and ubiquitously support delivery of quality care [14].

CDSSs have evolved noticeably over the past 25 years and will likely evolve and enhance just as dramatically or more so over the next 25 years [15]. According to a market research report by MarketsandMarkets [16], the global CDSS market size is expected to reach USD 1.8 billion by 2025 from an estimated USD 1.2 billion in 2020 at a compound annual growth rate (CAGR) of 9.1% during the forecast period.

CDSSs have successfully been implemented in a variety of settings and in different stages of the course of diseases. They have been utilized for non-communicable diseases such as cancer [17], neurodegenerative diseases [18], and comorbid chronic conditions [19], as well as for infectious diseases, like HIV [20] and COVID-19 [21].

It is essential to highlight the importance of considering the system-supported human decisions as the focusing endpoints rather than merely the stand-alone CDSS outputs, as it was pointed out by a recent systematic review [22]. CDSSs should be considered and evaluated as tool in the context of human-computer interaction and not as stand-alone clinician-replacement systems. Finally, raising the trust of clinicians in the utility and added value of these systems is of paramount importance [23].

This paper is organized as follows: The first section provides a brief overview of existing tinnitus-related CDSSs or models. The second section describes the aim and the context of our under-development CDSS. In the third section, the system's model and data are described. Finally, we present our future work and conclusion.

II. Related Work

In the literature there has been limited research on a CDSS for tinnitus. A brief review of current research progress on this topic is presented below:

- In [24], the authors describe in detail and in a step-wise fashion how to set up a network for an algorithm-based decision-making system in order to treat tinnitus and to assess the effectiveness of tinnitus treatment interventions. Specifically, they propose a knowledge discovery approach for a decision support system development and present theoretical concepts and algorithms for rule-based systems, including decision tables, classification rules, action rules extraction and meta-actions.
- In their technical report [25], Pryce et al. described the development of a decision aid for tinnitus care. This decision aid incorporates key evidence of efficacy for the most widely used interventions for tinnitus, along with information derived from patient priorities, when deciding which choice to make. The proposed decision aid has the potential to incorporate shared decision making between clinicians and patients.
- In another research [26], the authors developed a flexible temporal feature retrieval system which is able to group similar visiting patterns, with connection to an action-rules engine, and to observe intriguing and valuable outcomes on how the modification of treatment factors influence the changes of patient's recovery.
- An earlier paper [27] outlines a knowledge discovery and machine learning process and introduces several new temporal features to enhance tinnitus evaluation, outcomes analysis, and general comprehension. However, the research was in the early stages, and many opportunities exist for further analysis and learning.

In conclusion, research on a well-rounded CDSS for tinnitus is still in its infancy [28]. So far, the proposed CDSSs contain many methodological flaws, including lack of strict and well-defined inclusion criteria and barriers during their design [29].

III. UNITI CDSS

This paper is an overview of our CDSS for tinnitus, aiming at suggesting specific examinations and an optimal treatment strategy according to the individual patient's profile (Fig. 1). The proposed CDSS will be developed under the European research and innovation project "UNITI", which aims towards a unification of treatments and interventions for tinnitus patients [30]. More specifically, the primary objectives of the project's CDSS are to build trustworthiness in the evaluation and care of patients, to bring about precise assessment, to create standardization protocols for easy, practical and substantive patient profiling, and, mainly, to help in making efficient decisions for tinnitus personalized treatment and optimizing therapies plans.

UNITI's overall aim is to deliver a CDSS incorporating a predictive computational model attempting to address the

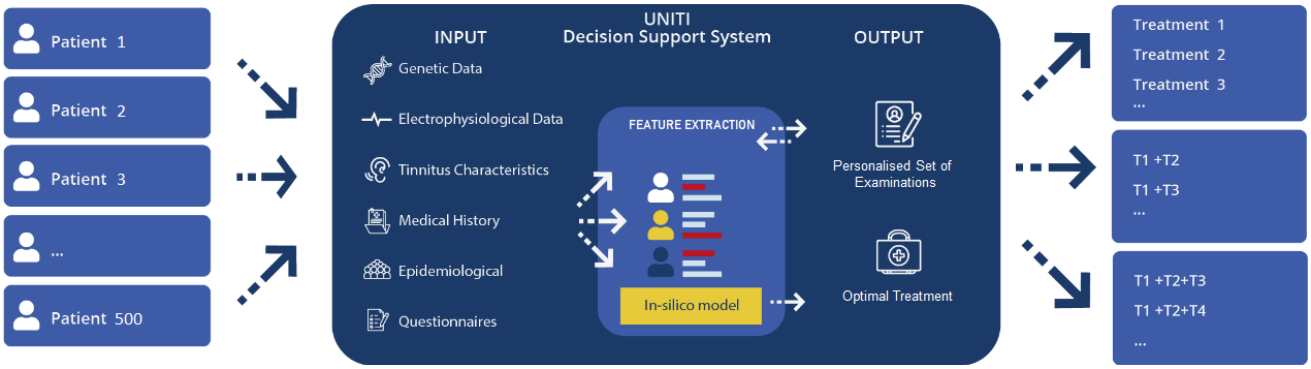

Figure 1. Overall concept of UNITI's CDSS

question which treatment approach (single or combination of interventions) is optimal for a particular patient based on their specific parameters. Along with this, an in-silico tinnitus-focused model of the inner-hair cell and the auditory-nerve complex will be developed, which description is beyond the scope of this paper. The CDSS' output will be used as a dynamic recommendation guideline at clinical or research level.

IV. Data and Models of the CDSS

In the context of UNITI project, a multicenter Randomized Clinical Trial (RCT - https://clinicaltrials.gov/ct2/show/NCT04663828) will be conducted, with a combination of the four widely-used interventions for tinnitus: cognitive behavioral treatment, sound therapy, structured counselling, and hearing aid fitting [30]. Actually, 500 patients - the largest number of participants so far in tinnitus research worldwide - will be recruited to the RCT and all their available parameters (Table I) will be systematically collected and stored in a common repository, the EU Tinnitus Database (EUTD - https://www.tinnitus-database.eu/).

These parameters (Table I) include medical and tinnitus related history, demographic and epidemiological data, and responses in questionnaires, assessing tinnitus severity and burden. Many parameters will be inputted by the patients themselves, through an interventional mobile app, able to map patient's tinnitus characteristics, produce individualized masking and music therapy (for those under this intervention plan) and record data in real time from each patient. If the existing patient's data are inconclusive, a personalized set of examinations will be proposed for them. These will include electrophysiological data, assessing auditory pathway function, and genetic testing, identifying a set of tinnitus associated genetic variants.

TABLE I. List of CDSS Input Data

Data Types & Subtypes		Features	Values
Tinnitus characteristics		Subjectivity	Subjective / Objective
		Duration	Acute / Sub-acute / Chronic
		Type / Character	Ringing / Buzzing / Tonal Hissing / Multiple / Other
		Span	Constant or Variable / Sporadic
		Pulsatility	Pulsatile / Non-pulsatile
		Laterality	Unilateral / Bilateral
		Annoyance	Bothersome / Non-bothersome
		Cause	Primary / Secondary
		Annoyance	Bothersome / Non-bothersome
		Triggers	Specification
		Tinnitus level	in dB
		Tinnitus matching	in kHz
Medical History	**Audiological assessment**	Audiogram (PTA)	Characteristics specification
		Tympanogram	Characteristics specification
	Ontological Symptoms	Otalgia	Yes / No
		Fullness of ear	Yes / No
		Otorrhea	Yes / No
		Vertigo	Yes / No
		Dizziness	Yes / No
	Comorbidities	Hearing Loss	Yes / No
		Auditory processing disorder (APD)	Yes / No
		Hyperacusis	Yes / No
		Vestibular disorders	Yes / No
		Imbalance / Fall	Yes / No
		Headache / Migraine	Yes / No
		Mood disorder	Yes / No
		Anxiety disorder	Yes / No
		Sleep disorder	Yes / No
		Depression	Yes / No
	Neurological & Vestibular function	Romberg	Yes / No
		Tandem Romberg	Yes / No
		Romberg by pillow	Yes / No
		Unterberger	Yes / No
		Dix–Hallpike	Yes / No
	Others	Medication / Drugs	Specification
		Surgeries	Specification
		Other diseases	Specification
Demographic & Epidemiological Data	**Demographic**	Sex	Male / Female / Other
		Age	in years
		Occupation	Specification
	Noise Exposure	Social	Yes / No
		Occupational	Yes / No
	Habits	Smoking	Yes / No
		Diet	Specification
Questionnaires	**Severity and negative impact of tinnitus**	Tinnitus Functional Index (TFI)	0 to 100 0-17: not a problem. 18-31: small problem. 32-53: moderate problem. 54-72: big problem. 73-100: very big problem
	Level of perceived tinnitus severity	Tinnitus Handicap Inventory (THI)	0 to 100 0-16: slight or no handicap 18-36: mild handicap 38-56: moderate handicap 58-76: severe handicap 78-100: catastrophic handicap
	Psychological aspects of tinnitus distress	Tinnitus Questionnaire (TQ)	0 to 84 0-30: slight 31-46: moderate 47-59: severe 60-84: very severe
	Tinnitus severity profile	Tinnitus Severity Questionnaire (TSQ)	0 to 40 (Higher scores indicating more severe tinnitus)
Electrophysiological Data	**Auditory pathway function**	Auditory brainstem response (ABR)	Characteristics specification
		Auditory Middle Latency Response (AMLR)	Characteristics specification
		Otoacoustic Emission (OAE)	Characteristics specification
Genetic Data	**Genetic predisposition to tinnitus**	Whole Exome Sequencing (WES)	Candidate genes (rare and common variants)
		Proximity Extension Assay (PEA)	Blood biomarkers

Primarily objective of the RCT will be the efficiency evaluation of interventions. Specifically, comparisons will be implemented between single and combinational arms, all different treatment groups, patients who received one treatment (single arm) versus patients in the combinational arm, who received this particular treatment together with any other possible combination, and all groups of patients who received a particular treatment both in the single and the combinational arm.

All the collected data from the RCT will be integrated in the project's repository (EUTD) and will be used for the purposes of training and validating the CDSS' models. As the data are large and complex, machine learning (ML) algorithms will be utilized to identify learning patterns in datasets, to classify the patient's profile, and to predict the patient's

response to each of the four interventions or to a combination of them. The fully-developed CDSS will be provided as an extra module in the existing interface of the EUTD which is currently used by the clinicians of all centers.

For the development of the CDSS model, open-source ML libraries (such as NumPy - https://numpy.org/ and Pandas - https://pandas.pydata.org/) will be used. The trained models will be integrated with the EUTD as a dockerized component which will have access on the data stored in RCT database.

V. Future Work – Conclusion

At this stage, the user requirements have been collected from all the stakeholders and the database schema has been defined. Many of the project's clinical partners have stored their retrospective data in the EUTD, which they will be utilized for the CDSS model initial fit on this dataset. The first version of the CDSS will be delivered during the running of the RCT, while the final version will coincide with the end of the project, integrating all the afore-mentioned parameters collected during RCT.

We hope that by developing and implementing this CDSS, we will be able to greatly improve the delineation and care of tinnitus, resulting in less distress and frustration for patients, their families, and clinicians alike.

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