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New Open Scenarios for STAT-ON™: The Medical Perspective

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Abstract

The chapter covers a transversal vision of the possible new scenarios where STAT-ON™ can positively contribute to helping professionals in the development of the clinical activity, and generate new possibilities in the treatments and patients' management.

7.1 Introduction

This chapter aims to provide a cross-sectional view of the possible scenarios for the use of the Holter STAT-ON™, from the perspective of medical practice, in the treatment and follow-up of patients with Parkinson's disease (PD). Today, there exists a practical unanimous agreement on the advantages and contributions that the proper use of technology implies in various aspects of our lives, such as health care. In the case of Parkinson's disease, and for reasons inherent to the disease itself, this possibility has been a little further from being able to become a reality, due to the nonavailability of the most suitable technology.

The STAT-ON™ solution opens up a good number of opportunities to make this contribution to improving the care and supervision of PD patients

effectively, always as a technological complement that provides objective and reliable information on the patient's motor status and its evolution, allowing the doctor to have a very correct vision of the patient's condition, in normal living conditions, thus going beyond the information that the doctor can observe in his office, at the time of the visit, or that can be provided by the patient himself, which on some occasions may be biased, qualitative, or imprecise.

In Chapter 6 several real cases were presented, corresponding to patients affected by PD and treated in different Spanish hospitals. In all cases, a presentation has been made of the contribution that the use of information obtained using STAT-ON™ has meant for the case. On many occasions, these benefits have been translated into better monitoring of the evolution of the disease, in establishing the appropriate criteria for a change in treatment or in improving the patient's own ability to become aware of the disease itself, allowing to establish a much more fruitful relationship with the neurologist.

The extrapolation of a series of cross-sectional conclusions has represented the possibility to establish the content that follows in the hereafter sections, and which leads to establishing the appropriate framework to glimpse a series of uses and future applicability of the STAT-ON™ device.

STAT-ON™ is conceived and marketed as a medical device for the detection and measurement of motor symptoms associated with PD. Therefore, it appears within the product specifications, it is capable of correctly detecting the appearance of dyskinesias, OFF states, and the presence of Freezing of Gait (FoG). However, as discussed below, the use that the professional can make of this information may be novel (for example, due to the existing correlation between the OFF states of the patient and the possible associated nonmotor-motor fluctuations (NMFs)).

Even though STAT-ON™ was conceived, tested, and proven from a database that included patients affected by Parkinson's who presented motor fluctuations (MFs) and were in intermediate stages of disease progression, it has been verified by the neurologists who have been using it that it can be useful in detecting the first MFs (which therefore affect inexperienced patients and who may have significant difficulty in describing them to their neurologists).

It has also been seen the importance that this technology can have in the correct identification of patients who are candidates to be users of technologically-assisted treatments (deep brain stimulation (DBS), infusion pumps, etc.), and their subsequent correct follow-up and necessary adjustment. Finally, STAT-ON™ can be a definitive aid for the more effective execution of clinical trials that require the participation of patients by filling in Hauser's diaries or personal symptom diaries. The sensor and the generated

report are good candidates to be an "electronic and automatic diary of the associated motor symptoms."

7.2 Detection of the First PD Motor Fluctuations

One of the main purposes of the use of the STAT-ON™ sensor is to help clinicians in the detection of the motor fluctuations (MFs). It is well-known, that traditional methods, such as a detailed clinical interview, validated clinical scales, or patient diaries can be useful [1–3]. Nonetheless, not all patients are always aware of their OFF time [4]. Some of the clinical cases described in Chapter 6, illustrate the real difficulties of PD neurologists when the clinicians need to go deeply into the MF details and the patients lack awareness of them.

The detection of the first MF can be a challenge, especially in the first years of the disease. The recommended wearing-off (WO) scales such as the 19-item *WO* or *Quick* questionnaires can increase the detection of WO in the setting of the daily clinical practice. However, it is not always possible for PD neurologists to use them in the daily-clinical practice scenario, mainly for the lack of time for each patient. Besides, the first appearance of MF (morning akinesia and WO) can be very subtle at the very beginning. The transition from a good motor state to a worst one can be gradual and ambiguous [1, 5]. While some patients can quantify and identify WO symptoms quite well, for others it is extremely difficult. Some studies that analyze the perception gaps between patients and physicians in terms of the detection of motor complications, show a lack of awareness of WO among PD patients [4].

Otherwise, several communication barriers can exist when explaining WO, such as patient's cognitive impairment, reluctance to discuss the symptoms, or caregiver absence [6]. To overcome all these challenges and barriers, wearable-sensor-based technology can help physicians to detect WO [7, 8]. Since the introduction of the STAT-ON™ in June 2019 in the setting of Spanish centers, PD neurologists are using this wearable to quantify the patient's OFF time [9]. However, the STAT-ON™ has been more widely used in advanced PD patients so far, being less explored the first phase of PD where the first MF emerges [9].

Even considering that the algorithms implemented in the sensor for the determination of the ON and OFF states and therefore the MFs were built with patients with advanced PD, and fully aware of their ON/OFF state (i.e., the learning database does not include patients who are not able to know and identify their motor status) [10], our preliminary results with the applicability of the STAT-ON™ to detect the first MF are very encouraging [5, 11–13].

In a retrospective analysis of 35 PD patients with a mean disease duration of 4.07 ± 1.0 years at the time of wearing the sensor, WO or morning-akinesia (MA) was suspected to occur by the neurologist but they were not well recognized by the patient or caregiver in 40% of the sample. Moreover, in 33.3% of the PD patients WO and MA were not suspected before wearing the sensor. After wearing the STAT-ON™ sensor, patient's and caregiver's self-awareness increased because in all the patients in whom WO/MA was not well recognized, the STAT-ON™ report showed the presence of them in all the cases. Among the patients who denied having MF/MA, the sensor detected them in 9 out of 10 patients. There were 6 cases in whom the STAT-ON™ report helped the patient/caregiver to understand that MF was occurring and recognized them. Still, three patients denied again having WO after wearing the sensor, but the STAT-ON™ showed it. In this line, another retrospective analysis focusing only on the MA of 28 PD patients, showed significant differences of the morning gait fluidity between patients without clinically suspected MA and those with MA clinically present and well explained and quantified for the patients [13].

All these preliminary results suggest that STAT-ON™ sensor is a promising and helpful tool for the neurologists who want to confirm the occurrence of the first MF. However, a critical issue that will need further study and clarification is the explanation for a disagreement between the symptoms and the sensor (i.e., when the sensor is detecting OFF or MA and the patient denies them). Besides, the well-known lack of awareness of the symptoms among patients or the simple fact that they minimize the symptoms, our hypothesis is that the sensor has a high sensitivity to detect a slowness of the gait fluidity before and after the levodopa intake. Hence, the sensor may be detecting this OFF transition before the patient is aware of it [5]. More studies in larger PD samples, addressing all these issues should be necessary.

7.3 Identification of Freezing of Gait and Falls

FoG is a frequent and disabling symptom in PD and a major risk factor for falls [14]. It is defined as sudden and usually brief episodes of inability to produce effective forward stepping that clinically occur during gait initiation or turning [15]. Detection of FoG is extremely important for PD neurologists for several reasons:

- Firstly, for classifying the type of parkinsonism and rule out and atypical parkinsonism or to identify a postural instability/gait difficulty

PD subtype, which is associated with a faster cognitive and motor decline [15].

- Secondly, to explore if the FoG is occurring in the ON or the OFF state, especially when selecting PD patients for DBS.
- Thirdly, for the implementation, as soon as possible, of a more adequate therapy, either pharmacological or nonpharmacological, and consequently try to prevent falls.
- Fourthly, to measure FoG reduction after pharmacological/nonpharmacological therapies. As seen in several cases of the previous chapter, it is well illustrated that FoG improves after initiating dopaminergic therapies.
- Finally, to detect longitudinally the appearance and progression of this disabling symptom that complicates the course of PD.

Besides the clinical information provided by the patient and the specific FoG scales, the sensor can serve as a complementary tool to detect the presence of FoG. In line to the detection of the first MF, the detection of the first FoG episode can also be a challenge. While in some patients FoG can be identified at the clinical examination or during the clinical interview, in some other instances the lack of time of the clinician for a proper identification of all the PD symptoms, can produce an underdiagnose of FoG. Moreover, another factor that accounts for an underdiagnosed FoG is that the patient's examination only reflects the motor state at a precise moment, without reflecting all the PD symptoms along a day [7].

For these reasons, wearable sensors such as STAT-ON™ are of great help. Our first experience **using the STAT-ON™ sensor for detecting FoG was that the sensitivity of the sensor was again extremely high**.

In our experience, in some cases it could be recommended to have "a daily-activities diary" while wearing the sensor (as it has been seen in the cases of Chapter 6). The use of this diary makes possible a more precise interpretation of the results when there is a possible disagreement (i.e., the STAT-ON™ reports a FoG but the patient denies its presence). We know that daily activities such as sweeping or "stop walking suddenly" can be detected as a FoG by the sensor, generating a "FoG false positive" that can be discarded or interpreted if such "daily-activities diary" is available from the patient. Still, a recently published pilot study with the STAT-ON™ in an unsupervised scenario showed that a 76.9% of agreement between the clinical interview and the FoG was detected by the sensor with a kappa coefficient

of 0.481 [5]. However, in this study FoG specific clinical scales were not applied.

In summary, using the STAT-ON™ sensor for all the purposes commented is worthwhile and several projects addressing these issues are ongoing.

7.4 Detection of Dyskinesias

Although recent and controversial views on the management of PD have suggested an overall decline of dyskinesia rates, the detection of dyskinesia is one of the main objectives when evaluating the PD patient [16]. Several reasons such as a more conservative use of levodopa regimes, the earlier introduction of DBS and other device-aided therapies, can account for the decline of these dyskinesia rates [16]. Nevertheless, and despite the negative results of a set of anti-dyskinetic agents, the clinical trials in the field of anti-dyskinetic agents are ongoing and STAT-ON™ could be of help as explained in this section.

STAT-ON™ has some limitations and cannot detect all the types of dyskinesia, for all the time because the sensor only detects the dyskinesia when the patient is not walking. Besides, the sensitivity and specificity are of 95% and 93% for strong or mild trunk dyskinesia while for mild upper limb dyskinesia the sensitivity is lower (39%) [17].

Despite that, our first experience using the sensor in clinical practice is that the STAT-ON™ can help the physician to improve the patient's awareness of dyskinesia. In several cases of the previous Chapter 6, it is shown that some patients mix up tremor and dyskinesia symptoms. Although the STAT-ON™ sensor cannot be used to detect tremor, it can be very helpful to detect dyskinesia when the patient thinks that "a dyskinesia confused as a tremor" is emerging. The procedure, then, can be to ask the patient to press the button of the STAT-ON™ when this situation is appearing.

In line with the previous aforementioned "false positives" possibilities with FoG (see section 7.3), in the case of dyskinesias, dancing, and housework are activities that can be easily confused with dyskinesia. For this reason, when discussing the report with the patient, it is important to review the patient's "daily-diary activities" to detect disagreements between the sensor and the patient.

Despite these challenges, detecting the first dyskinesias is a critical point during PD (similar to the detection of initial MF) because it indicates that the patient is entering a more complex phase of the disease and treatment adjustments are mandatory from this moment. Besides the use of the STAT-ON™ for measuring the effect of the treatment interventions, the sensor can also

help the clinician in the detection of the dyskinesias. However, further studies should be addressed to confirm the ability of the sensor in detecting the different types of PD dyskinesia.

7.5 Detecting Non-motor Fluctuations

In principle, many of the new wearable devices for monitoring the PD patients are focused on the detection of the related motor symptoms and, in general, they are considered as useless tools for detecting NMFs.

Despite the fact that STAT-ON™ is not designed to detect nonmotor symptoms (NMS), if the possibility of pressing the button to indicate a certain event is used correctly, it is possible to associate the presence of a certain period or motor state (e.g., an OFF state) with the onset of a state "in which the patient does not feel well" and which is normally associated with a nonmotor symptom condition. In this way, the patient could be instructed to tight the button when NMS appear, and it could be seen in the generated report if those moments have a correlation with detected OFF episodes. Then, STAT-ON™ could be used to identify NMF in an indirect way.

Our very preliminary experience suggests that when the patient complains of a NMF, the STAT-ON™ shows an OFF time detected [12]. This issue has also been illustrated in the previous Chapter 6 and future studies with STAT-ON™, analyzing the characteristics of the patient's OFF time, should be accompanied with the recommended clinical scales that complement the nonmotor part of the OFF state.

7.6 Selection of a Patient for a Device-aided Therapy and Monitor Response

Patients with Parkinson´s disease (PD) develop clinical fluctuations and their identification is very important because these patients have a worse status in terms of motor symptoms, non-motor symptoms (NMS), quality of life (QoL), and autonomy for activities of daily living (ADL) [18]. For example, in the DEEP study [19], wearing-off was detected by the neurologists in more than 20% of the patients in the subgroup with fewer than 2.5 years of disease duration, while with the WOQ-19, 41.8% of patients were detected. Motor symptoms and NMS can be present during the OFF episodes [20] and different instruments could be useful for detecting clinical fluctuations in PD: (1) asking directly to the patient; (2) scales or questionnaires; (3) ON–OFF diaries; (4) wearable tools; (5) website applications; (6) video recording (at home or at the consult).

In this context, effective management of PD is critical at all stages of disease, requiring individual customization of therapy including optimization of oral regimens and consideration for nonoral treatments such as advanced device-aided therapies (i.e., DBS, levodopa infusion, and/or apomorphine infusion) [21]. A lack of consensus around the definition of advanced disease leads to delays in the identification of advanced PD patients, and the correct managing disease progression and its timely treatment [22]. Some tools have been proposed to identify patients inadequately controlled on oral medications such as de 5-2-1 criteria [23–25], the CDEPA questionnaire [26], and the MANAGE-PD [27]. Specifically, the MANAGE-PD provides information about if a patient could be a candidate for a device-aided therapy and despite some limitations its clinical use may complement clinician treatment decision-making and facilitate timely identification and management of PD symptoms [27, 28].

STAT-ON™ could be a tool to help the neurologist when deciding if the patient is a candidate for device-aided therapy as well [29]. Many factors are relevant for deciding if a patient is a candidate for a device-aided therapy. One of the most significant is the total time the patient is in OFF state during the waking day. OFF episodes can be detected with the STAT-ON™ with high sensitivity. The ON/OFF algorithm was also validated against the Hauser diary showing a greater compliance (37% records more were achieved by the sensor) and a high accuracy (positive predictive value 0.92; negative predictive value 0.94) [30].

Recently, a subanalysis of the MoMoPA-EC clinical trial showed a moderate concordance between the STAT-ON™ and the patient diary, but the correlation between the different UPDRS indices was better with the STAT-ON™ than with the Hauser diary [31].

In 2020, Santos-García et al. published the opinion of 27 clinical experts on PD about the STAT-ON™ after having tested the device in clinical practice [32]. A total of 119 evaluations were performed and the STAT-ON™ was considered better than diaries and a useful tool to detect advanced PD by 70.3% and 81.5% of the neurologists, respectively. Moreover, other important signs that can be appearing or increased during the OFF episodes can be detected with the STAT-ON™ such as bradykinesia, freezing of gait (FoG), and falls [33]. Time with dyskinesia is detected with the STAT-ON™ as well.

Some NMS such as pain, fatigue, bad mood, or anxiety can appear during the OFF episodes and improve with a device-aided therapy, so their identification is of great importance [34–36]. These NMS can be indirectly detected with the STAT-ON™ by asking the patient to press the button of the sensor (see above section). All the information collected with the STAT-ON™,

together with other factors that are considered when deciding if the patient is a candidate for device-aided therapy (i.e., age, family support, comorbidity, cognitive function, etc.), should finally be taken into account.

In summary, the STAT-ON™ could help the neurologist to know about 3 key factors for deciding if a patient is a candidate for a device-aided therapy:

- Time in the OFF state during the waking day.
- Symptoms during the OFF episodes (correlation between records and clinical assessment).
- Severity of OFF episodes (correlation between records and clinical assessment). Specifically, it must be considered the obtained data about OFF episodes, dyskinesia, FoG, falls, and gait problems.

If the patient is finally treated with a device-aided therapy, the STAT-ON™ could be useful for monitoring the response with the new therapy, both in the short- and the long-term. The comparison of records (before vs. after starting with the device-aided therapy) will allow the neurologist to observe the reduction in OFF time and the changes in other variables, as well as long-term monitoring of the patient's condition and the identification of possible therapy adjustments.

The device has been also validated with advanced-stage PD patients with levodopa-carbidopa intestinal gel (LCIG). Bougea et al. demonstrated the better detection of ON/OFF motor fluctuations, dyskinesia, and falls against patients' diaries in 51 patients with advanced PD [37]. All the sensitivities and specificities were higher with the sensor rather than with the diary, concluding that STAT-ON™ can be a promising tool for monitoring patients with advanced disease.

In another study, the STAT-ON™ was used to monitor a patient with LCIG therapy whose motor symptoms were worsening after 4 months of using LCIG therapy. STAT-ON™ was used to check his state and it was detected a bad adjustment of the LCIG tube. After the correct adjustment, the STAT-ON™ was used again to check the improvement on motor states [38].

STAT-ON™ was also used in patients who were administered with PERCEPT™, a deep brain stimulator that also registers the signal perceived from the subthalamic nucleus field, remarkably aligning their signals in the appearance of OFF states, ON states, dyskinesia, and FoG episodes. This case study suggests that STAT-ON™ can be a useful tool for the optimization of this kind of therapy [39].

Another pilot analysis conducted in 11 PD patients, 4 of them with deep brain stimulation, suggested that STAT-ON™ could be useful to have

an objective measurement of the motor status of patients in advanced stages of the disease, with difficulty in controlling motor symptoms, inconsistencies in their daily reports, suspicion of inappropriate taking of medication, and in those who were enrolled to a treatment of greater complexity such as surgery [40]. In patients under apomorphine infusion the STAT-ON™ can be a useful tool [41] and in the future could be used in patients receiving new drugs such as subcutaneous levodopa infusion or drugs for rescuing the patient from the OFF state with the aim of monitoring the response. In line with this, other projects using the STAT-ON™ in advanced PD patients, such as the GATEKEEPER project, are ongoing [42].

7.7 Monitor the Response to a Treatment

As it has been already explained and commented in above text, the STAT-ON™ can be used for monitoring the response of a device-aided therapy or other drugs prescribed with the aim to reduce the OFF time in a patient with PD. Clinical fluctuations are very frequent [43] and many options are available for trying to optimize the status of the patient [44]:

- to adjust levodopa,
- to add a dopamine agonist,
- to add a catechol-O-methyltransferase inhibitor, and
- to add a Mmonoamine oxidase-B inhibitor.

In practice, many patients receive all these drugs added to levodopa and it could be helpful and of great interest to monitor with the STAT-ON™, the motor status of the patient before and after starting with the drug selected.

A correlation between the perception of the patient about the effect of the drug over the symptoms and the change in the record collected with the STAT-ON™ would be important information. Even regular monitoring could be used for trying to be more sensible to detect changes in the status of the patient over the time with the aim of adjust the medication early. In all these cases the focus should be the OFF state and symptoms related to the OFF episodes.

A very interesting alternative could be to use STAT-ON™ to monitor dyskinesia in PD patients. The effect of amantadine or other adjustments and/or therapies [44] conducted with the aim of improving dyskinesia could be monitored, again with a comparison between the record before and after starting with the drug. Specific disruptive complications for the patient such

as FoG or falls could be also monitored, before and after an intervention with a drug or a dispositive (visual clues, etc.) or other type (physiotherapy, etc.).

Even in PD patients without motor fluctuations the STAT-ON™ could be useful for monitoring the effect of exercise programs over aspects related to gait and daily physical activity. Finally, and very importantly, the use of new wearable sensors such as the STAT-ON™ could be especially useful in patients with mild cognitive impairment or dementia [45], since the data collected with the Hauser diary may be unreliable in these patients.

7.8 Use in Clinical Trials

Currently, there is an ongoing trial with the STAT-ON™ entitled MoMoPA-EC [46]. The objective of this trial is to show whether using the Parkinson Holter (STAT-ON™) is better than the clinical interview used in traditional clinical practice (primary objective), and whether it is not inferior to the ON-OFF diary recorded by the patients at home (exploratory objective). This is a multicenter (43 centers from Spain) randomized with parallel assignment and triple masking (participant, investigator, and outcomes assessor). The primary outcome is the change from baseline to the last visit in daily hours in the OFF state.

Regarding all previous comments about the STAT-ON™ and Hauser diaries, it could be of great interest the progressive introduction of the STAT-ON™ as a tool for measuring the change in the OFF time in those clinical trials conducted in PD patients with MFs. The change in the OFF time from the baseline visit to the final visit measured with the STAT-ON™ could be used as the primary endpoint in trials with a drug for reducing the daily OFF time. Its use would be easier for the patients and the possibility of recording the data even about all the days without a fatigue effect compared to the diaries would be a positive point. Depending on the trial and the endpoint, other variables could be monitored: time with dyskinesia, presence of FoG, falls, etc. Moreover, and regarding advanced PD and symptomatic interventions, the STAT-ON™ could be used for monitoring the effect of device-aided therapies in the context of clinical trials.

Another possibility to explore could be the use of the STAT-ON™ in clinical trials with molecules with a potential modified disease effect. In some trials (drug vs. placebo) the time to motor worsening or the time to starting with levodopa are included as secondary variables and the STAT-ON™ could provide a more objective information about the progression of motor symptoms. Even in open label trials with some therapies (grow factors, cell therapy, etc.), the development of some complications such as OFF episodes,

FoG, falls, or dyskinesia could be defined as endpoints in the very long-term follow-up. In general, the use of new technology is the rule in trials with a disease-modifying molecule with the aim to know more precisely the changes that occur in the disease and be able to compare between placebo and the drug [47].

Finally, the STAT-ON™ could be used as a helpful tool not only in double-blinded clinical trials but also in phase IV studies providing information about clinical real-world evidence. Data about real-world evidence is of great importance after starting with the commercialization of a novel molecule and the use of wearable sensor platforms, smartwatches equipped with accelerometers and other wearable devices could be used for getting very important information [45, 48–53].

7.9 Use as a Marker of Disease Progression

As it has been previously commented, new devices can be used to monitor the progression of the disease. The development of MFs can be considered a turning point in the story of a patient with PD because some therapies in fact are indicated only in patients with levodopa and fluctuations [44]. The STAT-ON™ could be used for trying to detect early predictable fluctuations (morning akinesia; wearing-off), and also in the long-term, to monitor an increase of the daily OFF time or the development of unpredictable motor fluctuations such as no-ON or partial-ON during the afternoon/evening.

Keeping in mind the concept of motor fluctuations development as a turning point, an interesting idea could be to compare the record collected with the STAT-ON™ in early PD patients (i.e., <5 years of disease duration from symptoms onset) in patients with positive vs. negative 5-2-1 criteria [23, 24]. Moreover, the detection and monitor progression of other complications such as FoG, falls, or dyskinesia could be conducted with the STAT-ON™ in the medium- and long-term.

7.10 Research and Future Scenarios with STAT-ON™

The focus of remote technologies is now slowly shifting toward the broad, but more “hidden,” spectrum of NMS [54]. To apply technologies in prospective cohorts [55] with the aim of obtaining very valuable data seems to be an interesting approach. Recent clinical research provides growing evidence that various NMS such as neuropsychiatric, autonomic, and sensory symptoms (particularly pain) also show fluctuations in patients with motor fluctuations

(called NMF) [20]. This aspect cannot be directly assessed specifically with the STAT-ON™, but it is also known that NMS burden is greater in PD patients with motor fluctuations [18] and the relationship between NMS and motor fluctuations can be explored with the STAT-ON™ combined with data collected applying validated scales (e.g., Non-Motor Symptoms Scales, Non-Motor Fluctuation Assessment Questionnaire, etc.) [56].

Integration of the telemedicine in the management of PD could be useful to remotely monitor the PD motor complications, facilitate the access to care, complement, or replace the in-office consultations specially when these are not possible for geographical reasons, improving the detection of patients who are candidates to a device-aided therapy and facilitate the monitoring of device-aided therapies [57–59]. Moreover, the STAT-ON™ can be used as a part of a multidisciplinary telemedicine intervention with the aim of reducing the risk of some complications such as falls [60]. Even the information of the STAT-ON™ can be complementary to the other devices [61] and all together useful for making decisions about the treatment of the patient with PD. In the future, it would be of great interest to apply the use of the STAT-ON™ and other devices in longitudinal follow-up cohorts [55].

7.11 Conclusion

It can be stated that the role of STAT-ON™ complementary technology is clear, providing objective information on the motor state of PD patients, which the neurologists can use to complement their own observations, helping them to make decisions, in many cases, much more substantiated. This enables a more accurate prescription, directly impacting in the QoL of the patient. The use of STAT-ON™ in clinical practice for evaluating better PD patients, for selecting better and earlier the candidate patients to specific therapies, the use in clinical trials seems to be scenarios where STAT-ON™ fills a gap which seems to be beneficial for the clinician and for the patient. Additionally, the continued use and the experience acquired by a significant number of neurologists give rise to being able to define future and new fields of application.

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