MICROSENSOR TECHNOLOGY TO EVALUATE PATIENT ADHERENCE WITH REMOVABLE ORAL APPLIANCES

by

Stacey Jenna Kirshenblatt

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Abstract

Objective: The aim of this study was to evaluate the accuracy of three thermosensitive microsensors, which record "wear-time" of removable oral appliances (OA) used for orthodontics and obstructive sleep apnea therapy.

Methods: *In vitro* testing was undertaken for TheraMon (Sensor T, n=20), AIR-AID SLEEP (Sensor A, n=30) and DentiTrac (Sensor D, n=16) microsensors, which were placed in a water bath to simulate "wear-time" of OA. Logs of when the microsensors were placed in the water bath were compared to the time readouts from the microsensors. Trial 1 examined the accuracy of long durations of "wear" (7 hours/day). Trial 2 examined short durations of "wear" (2 hour intervals). Trial 3 tested the impact of different embedding materials on accuracy: acrylic, polyvinylchloride and thermoactive acrylic. *In vivo* testing included 14 volunteers who wore maxillary retainers embedded with Sensor A and D for 30 nights. Subjects' logs of appliance usage were compared to the computed readouts from the sensors.

Results: In the *in vitro* phase, the median absolute deviation of the computed "wear-time" minus the logged time was 0.00 minutes for Sensor A and Sensor T in all trials. For Sensor D, the median deviation was 5.00 minutes in trial 1 and 3 and 10.00 minutes in trial 2. Sensor A was significantly more accurate than Sensor T and Sensor D in trial 1 ($p<0.001$). In trial 2, Sensor A and Sensor T were equal in accuracy but were significantly better than Sensor D ($p<0.001$). In trial 3, there was no effect of the material on the recording accuracies of Sensor A ($p=0.13$) and Sensor D ($p=0.41$); Polyvinylchloride was found to be significantly less accurate for Sensor T

(p<0.05). In the *in vivo* phase, the median absolute deviation of Sensor A was 3.00 minutes and Sensor D was 5.00 minutes; there was no significant difference between Sensor A and Sensor D (p=0.45).

Conclusion: Sensor D tended to have the largest deviation in recording accuracy in *in vitro* testing using the water bath. All three microsensors have acceptable clinical accuracy and can be used to record "wear-time" of removable OA fabricated from different materials.

Preface

This research project was designed by Dr. Stacey Kirshenblatt under supervision of Dr. Fernanda Almeida and the guidance of Drs. Hui Chen, Alan Lowe and Ya Shen. The data was collected and analyzed by Dr. Stacey Kirshenblatt who prepared the manuscript with advice from Drs. F. Almeida, H. Chen, A. Lowe, Y. Shen and D. Ruse. The project was supported in part by royalties paid to the University of British Columbia. The microsensors tested were donated from TheraMon (Handelsagentur Gschladt, Hargelsberg, Austria), AIR AID SLEEP (AIR AID GmbH & Co KG, Frankfurt, Germany) and DentiTrac (BRAEBON Medical Corporation, Kanata, Ontario). The study was approved by the University of British Columbia office of Research Services, Humans Research Ethics Board (Certificate Number: H12-00855).

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AHI	Apnea and Hypopnea Index
CPAP	Continuous Positive Airway Pressure
IR	Infrared
MAD	Mandibular Advancement Device
OA	Oral Appliance
OSA	Obstructive Sleep Apnea
PVC	Polyvinyl Chloride
RFID	Radio Frequency Identification Device

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Dedication

For my parents…

Thanks for your years of encouragement.

Chapter 1: Introduction

Successful orthodontic treatment with removable oral appliances (OAs) is impossible without cooperation and motivation of patients. Failure to adhere to the prescribed wear schedule of a removable OA may result in a slow to no treatment response.[1] In the field of sleep medicine, removable OAs are becoming an increasingly popular alternative to continuous positive airway pressure (CPAP) for the treatment of obstructive sleep apnea (OSA). These appliances are very similar in design to functional appliances used commonly for growth modification in orthodontics. The appliances can be inserted and removed by patients, thus placing responsibility on the patient to follow a prescribed wear schedule regimen.

To date, there have been many scientific publications that have addressed the issue of adherence in dentistry and sleep medicine, in an effort to determine how to improve and monitor patient adherence.[2-13] It has not been possible to objectively determine, based on evidence, the wear-time necessary to achieve successful results. This is because objective data measuring wear habits of removable OAs in patients was very limited.[14, 15] Rather, researchers and clinicians are forced to rely on patients' subjective views of their own compliance, which is often overestimated. This thesis reviews the factors affecting adherence in both the field of dentistry and sleep medicine. The main scope of this work was to test the use of objective microsensor technology to measure adherence in patients using removable OAs.

1.1 Definitions

R.B. Haynes defined compliance as it relates to health care as the "extent to which a person's behavior (in terms of taking medications, following diets, or executing lifestyle

changes) coincides with medical or health advice".[16] While the term compliance may be associated with a negative connotation of a patient's will being submissive and the clinician in a position of authority, the term "adherence" has been deemed more appropriate. Adherence places more the burden on the clinician to assume responsibility for the patients' cooperation with the treatment regimen.[12, 16, 17] Adherence reflects the realization that patients need to play an active role in their treatment in order for it to be successful.[18] While the terms compliance and adherence are used interchangeably throughout the literature, for the aforementioned reasons, adherence will be used in this thesis.

1.2 Determinants of adherence

Adherence is a fundamental component in ensuring successful treatment with removable OAs. Many of the appliances used in orthodontic practice rely on patients to wear them as prescribed. Headgears, removable retainers, functional appliances and OAs for OSA are inserted and removed by patients themselves. To ensure efficient clinical management of patients, researchers have attempted to identify patient factors that would help clinicians predict the level of adherence.

The literature examining adherence rates to treatments for OSA is limited in the area of OAs. Due to the lack of objective means to measure adherence, clinicians must rely on subjective self-reports of adherence. There is very little research on the factors affecting adherence for OA therapy for OSA. A greater amount of research, however, has been done on adherence with CPAP therapy.[8, 11-13, 19-24] With the advent of adherence monitors that could be incorporated into CPAP machine, researchers and clinicians are able to determine adherence using objective metrics.

1.2.1 Psychosocial aspects

Considerable attention has been devoted to the examination of personality characteristics as a method to predict patient subjective adherence in orthodontics.[1, 2, 25-32] Adherent patients are characterized as enthusiastic, energetic, outgoing, self-controlled, responsible, trusting and hard working.[33] These patients tend to have better grades in school, are considered academically brighter and show less deviant behaviour in school.[34] On the contrary, non-adherent patients are described as hard-headed, independent, temperamental, impatient, individualistic and intolerant of prolonged effort.[33] Based on these grounds, a patient's scholastic performance in school may serve as a useful tool in estimating adherence. However, children who are of below-average intelligence do not necessarily show poor adherence. This is because there are many variables that depend on a number of other psychosocial factors.[34]

Many clinicians believe that non-adherent behaviour is the result of a non-adherent personality trait.[18] This belief allows clinicians to "blame" the patient for unsuccessful treatment. However, the search for a non-adherent personality has been largely unsuccessful.[18] There is little to support the notion that patient characteristics are reliable predictors of adherence. As well, studies have found that patients often adhere with some parts of a treatment regimen but not with others. For example, a patient who keeps his/her appointments and has excellent oral hygiene may not wear the appliance as prescribed. Thus, adherence appears to be specific to each behaviour and task and is not reflective of a specific characteristic of a patient that can be generalized.[18, 35]

There are many studies published addressing psychological assessment of adolescent patients undergoing orthodontic treatment.[26, 28, 29, 36, 37] Southard et al[29] examined the application of the Millon Adolescent Personality Inventory (MAPI) in evaluating orthodontic adherence. The

MAPI is a 150-item questionnaire that is used primarily in adolescence to assess eight personality styles. From surveying 100 participants, age 13 to 18, the study concluded that MAPI has potential to be a useful instrument in assessing adolescent adherence and the management of adolescent patient behaviour in orthodontic practice. However, it may not be feasible to administer a 150-item questionnaire in non-research related environments. Cucalon and Smith[36] administered to 250 patients, age 11 to 17, three standardized psychological tests: The Comprehensive Personal Assessment System Self-Report Inventory, The Adolescent Alienation Index and The Home Index. They found that adherent patients scored higher on self-esteem, derived self-satisfaction from personal achievement, were optimistic regarding the future, had higher socioeconomic status and had a low degree of general alienation from society. According to this study, these brief psychological inventories are easy to administer and could be helpful to clinicians in anticipating adherence problems during orthodontic treatment. El-Mangoury[26] used psychological instruments in order to measure achievement, affiliation and attribution motivation. From the sample of 70 orthodontic patients, she concluded that high-need achievers, high-need affiliators and those with internal motivators cooperate better in orthodontic treatment. She stated that "[t]he results obtained from this study indicate that orthodontic cooperation is predictable through psychological testing".[26]

In comparison, there are other studies that demonstrated that psychological testing alone could not predict patient adherence to orthodontic treatment. Lee and Kim[37] surveyed 561 patients, age 10 to 22, from Seoul, Korea, before and after treatment using two types of locus of control questionnaires: Rotter internal control scale (RICS) and Nowicki-Strickland external control scale (NSECS). They found that there was no difference in the profiles of good and poor adherent patients. They concluded that patient adherence is complex and cannot be predicted by

locus of control evaluations before orthodontic treatment. Woolass et al[30] surveyed 1,018 patients, their parents and teachers. They examined 147 variables and only found 10 that showed a significant difference between poor and good cooperators. This indicates that the use of long socio-psychological questionnaire is uneconomical. As well, the authors noted that their measurement of adherence was subjective and that the use of an objective adherence monitor would strengthen the results of the study. Nanda and Kierl[28] questioned 100 patients and 131 parents in order to explore psychosocial factors such as the patients' and parents' treatment attitudes and expectations, as well as the relationships between patient, parent, and orthodontist. From all of the parameters tested, only orthodontist's perception of the orthodontist-patient relationship had a strong association with patient adherence. This indicates that the development of an effective relationship early on in treatment between orthodontist and patient could be beneficial for future adherence. The study concluded that neither personality tests, surveys on orthodontic attitude, nor the patient's orientation towards their peers were significant predictors of patient adherence.

Personality traits have also been explored as a determinant of adherence in CPAP therapy. It has been reported that depressive and hypochodriacal personalities were associated with poorer adherence. On the other hand, patients who enjoy daily activities and do not rely on avoidant behaviour for coping strategies were more cooperative with CPAP therapy.[11, 12] A systematic review of CPAP adherence described the typology of adherent users as those who identify the risks of OSA, identify the expected outcomes from the onset, have few barriers, develop and define goals for CPAP use, have a positive belief in the ability to use CPAP and have social influences that are prominent in their decision to pursue diagnosis and treatment. On the other hand, non-adherent CPAP users are unable to define risks associated with OSA and do

not describe expectant outcomes because they have a low belief in their ability to use CPAP. They describe negative experiences early in treatment which reinforces this belief that they cannot use CPAP.[11] Therefore, a patient's "readiness" and confidence in CPAP therapy is associated with increased adherence to treatment.[12]

The social cognitive theory has frequently been cited to explain factors of adherence. Based on this theory, an individual is more likely to take a preventive action if he/she believes that the benefit outweighs the cost and if he/she has a sense of self-efficacy.[12] The Self-Efficacy Measure for Sleep Apnea (SEMSA) was designed by Weaver et al[19] to assess adherence-related cognitions in patients with OSA prior to the initiation of CPAP therapy. The questionnaire examines three major cognitions that influence health-promoting behaviour: risk perception, perceived expectations and treatment self-efficacy. A study examining 213 subjects with newly diagnosed OSA found SEMSA had strong psychometric properties. It has the potential to be used as a valid and reliable instrument to identify patient perceptions and could indicate who is likely to be adherent to therapy.[19] De Zeeuw et al[21] interviewed 85 consecutive patients prior to the initiation of CPAP therapy using four standardized questionnaires: Nottingam Health Profile, von Zerssen's Depression Scale, State Trait Anxiety Inventory and the Internal, Powerful Others and Chance (IPC) Scale. They found on follow-up that individuals who discontinued CPAP therapy had a diminished external locus of control and could not be convinced of the necessity of CPAP by their health care professional. Thus, identifying patients with a reduced external locus of control belief prior to therapy may help identify non-adherent patients from the onset. No studies have been published on which psychosocial traits may affect adherence with OA for OSA.

1.2.2 Gender

Patient gender is a common factor cited as a predictor of adherence. Some literature suggests that there is greater adherence with orthodontic removable appliances amongst girls compared boys.[28, 36, 38, 39] Girls may have a higher level of adherence because they tend to have lower self-esteem and are more likely to be displeased with their dental appearance. This may help motivate girls to seek treatment. However, this may also prevent the same patients from wearing overly visible orthodontic appliances in public, such as a headgear.[34] As well, girls tend to mature earlier than boys and, therefore, may have a more adult perspective and attitude towards orthodontic treatment.[39] In contrast, there are many studies that have failed to show gender as a significant factor in predicting adherence.[2, 28, 32, 40-43] Much of these previous findings relied on subjective measures of adherence, such as orthodontists' judgment, which may be more a reflection of social and gender stereotypes than a valid correlation.[28, 36, 39-41] Studies using objective measures, such as electronic sensors, have found no difference in adherence between genders.[2, 32, 43, 44]

Similarly, the evidence remains unresolved regarding gender-related differences in CPAP adherence. Sin et al[22] found that women used CPAP more frequently than men. However, Pelletier-Fleury et al[8] and Woehrle et al[45] described the female gender as a factor significantly associated with non-adherence with CPAP therapy. Ye et al[23] observed no gender differences in CPAP adherence. There have been no studies examining gender differences solely related to adherence with OA therapy for OSA. Long-term discontinuation of OA treatment has not been found to be different between genders.[46, 47]

1.2.3 Age

Age is often considered a very influential factor in adherence. Allan and Hodgson[33]

reported that age is the single best predictor of patient adherence in orthodontics. Younger patients are more cooperative than older patients.[2, 3, 5, 31, 43, 48-50] Weiss[49] and Bos[43] found that children under the age of 12-13 were most cooperative. The importance of parental involvement in patient adherence cannot be ignored. While younger children are found to be more cooperative patients, this may be explained by the increased parental involvement in young patients' treatment. Older children have a higher degree of internal motivation and less need for parental support.[50] Bartsch et al[2] found that an external locus of control, especially if parental, was closely related to adherence. Colenaty and Gabriel[31] found that younger patients, under the age of 14, who have low ego strengths and external locus of control is highly predictive of adherence but not in adolescents. Cooperation is difficult for many adolescents. Teenage years are typically a time of emotional turmoil associated with puberty. It is at this time that adolescents solidify their values and goals, become less dependent on parents and often rebel against parental influences. As well, adolescents may not recognize the detriments and risk of not complying with a certain behaviour or treatment regimen.[3] Thus, adherence with appliance wear steadily becomes more of a problem up to the time of commencing puberty.[2] While some studies have found increased cooperation in adherence with young, pre-pubertal patients, other studies have found no difference.[3, 28, 32, 40, 41, 44, 51] The variation in the literature on the effect of age on adherence may be confounded by children's individual psychological maturation. It is likely that patient adherence is complex and cannot solely be explained by a patient's age.[34, 37]

Age as factor for CPAP therapy was examined by Woehrle et al[45] who retrospectively examined a cohort of 4281 patients using CPAP. They found that the use of CPAP was high in all age groups and tended to increase with increasing age. Patients over the age of 60 used the CPAP for 20 minutes longer than those under 60 years. There were both fewer nights without

therapy and longer average use per night in the older population. This may be explained by disease severity, which was not examined in the study. Disease severity may increase with age and adherence to treatment is dependent on disease severity. While age difference was found to be statistically significant, these differences are small and not clinically relevant. Pelletier-Fleury et al[8] examined 163 patients using CPAP and found that there was no independent effect of age on adherence with CPAP therapy.

A systematic review published by Sawyer et al[11] found that early studies on CPAP treatment in children reported adherence to be generally high. However, these studies relied on self- or parental-reports of CPAP use. More recent studies, using objective measures of adherence have found less than optimal CPAP use in this population. O'Donnell et al[52] found that children aged 13-18 years and those under 6 years were less likely to accept CPAP treatment than children 6-12 years old. Studies suggest that adherence to CPAP therapy in children is affected by age, maternal education, mask style, length of time of initial acceptance of CPAP, higher self-reported quality of life and lower body mass index.[11] Age as a factor of OA therapy adherence has yet to be explored, although the long term discontinuation of treatment has not been found to be dependent on age.[46, 47]

1.2.4 Socioeconomic status

The potential influence of a patient's socioeconomic status on cooperation and adherence has been addressed and debated in the literature. It has been proposed that patients belonging to families of higher socioeconomic status are more cooperative orthodontic patients.[3, 36] This may be explained by differences in the value of facial esthetics. Higher socioeconomic groups perceive dentofacial appearance to be highly important for social and occupational success.[28, 34]

On the other hand, patients from lower middle class families are also reported to show increased adherence compared to upper class families. This may be attributed to the greater need for social acceptance, higher social aspiration, better child-parent relationships and greater value for money seen in these socioeconomic groups.[53] There are many studies which reported no difference in patient adherence based on socioeconomic status.[18, 28, 51, 54] A study examining the rate of adherence comparing Medicaid versus self-paying orthodontic patients at the University of Connecticut Health Centre Orthodontic clinic found no significant difference in adherence between the groups, indicating that socioeconomic status does not appear to play a role in orthodontic treatment adherence.[54] However, recently, a study that used objective microsensors to record adherence rates with orthodontic retainers, found that patients who had government funded health insurance wore their appliances significantly more, by an average of 3.4 hours, that those who had private insurance.[44]

Socioeconomic status appears to play a very influential role in adherence to CPAP therapy. Simon-Tuval et al[24] reported that patients with lower socioeconomic status were less likely to accept and commence CPAP treatment. Patients living in poorer neighborhoods were associated with non-adherence. This may be explained by increased likelihood to smoke, excessive drinking, poorer diets and the difficulty in affording CPAP treatment for patients with lower socioeconomic statuses.[12] In an Israeli study by Brin et al,[55] they found that those in the highest income brackets purchased a CPAP machine 62% of the time, while those in the lowest income bracket purchased the machine only 28% of the time. It has also been found that CPAP users who live alone are less likely to be adherent than those who live with someone. Sleeping with a spouse or partner has been found to increase adherence as they may provide feedback regarding the elimination of symptoms, such as snoring, which may increase CPAP use.[20]

1.2.5 Cultural differences

Several studies have examined the influence of cultural differences and race in orthodontics. Such studies examined cultural differences on the perception of orthodontic treatment need.[56-59] Dental esthetics have also been found to be judged differently by different ethnic groups.[57, 60-65] However, there is no literature examining cultural differences in regards to adherence to orthodontic treatment.

There is very little literature examining cultural, racial and ethnic differences in area of adherence in the field of sleep medicine. While only Caucasians and African Americans have been examined, there is some evidence to suggest that African-Americans were five-and-half times less likely to be adherent than Caucasians.[13, 20] The reasons for this difference between race was not examined and may be more related to socioeconomic status and health literacy.[13, 20] Practitioners in Canada, which is a very multi-cultural country, would greatly benefit from further research in this area in both dentistry and sleep medicine to better understand and predict patients' adherence.

1.2.6. Treatment efficacy and side effects

Removable appliances may have side effects that impact patients' adherence. In a study[66] with 84 patients treated with removable appliances, 81.9% complained of impaired speech, 61.4% lacked confidence in public, 54.1% had impaired swallowing and 10.8% reported difficulties with breathing. Most of these concerns were alleviated by day seven. However, lack of confidence was significantly associated with decreased adherence to treatment. In another study[67], it was found that acceptance of orthodontic appliances and adherence to treatment may be predicted by the amount of initial pain and discomfort experienced. On the contrary, one

research found that adherence could not be predicted on the discomfort at the beginning of treatment, yet, aversion to wearing the appliance in public was related to patient adherence.[68] The investigation of related side effects of removable orthodontic OA and its correlation to adherence using objective measures has not yet been explored.

In the field of sleep medicine, one of the main reasons for non-adherence and terminating OA therapy is due to the patient's perceived treatment efficacy and side-effects related to long term continue use of therapy. Studies on long-term adherence of OA found that 44.9-86% of patients reported the discomfort as the number one reason for discontinuing OA therapy. No or little effect on symptoms was the second reason cited by 22-36% of patients.[46, 69] Patients who discontinued treatment within the first six months of OA frequently reported words such as "uncomfortable" and "inconvenient" to describe the treatment. Those who continued treatment for longer than six months reported "changes in occlusion" as concerns.[46] However, others have reported that the dental side effects that occur with frequent OA usage are unimportant compared to the reduction in daytime sleepiness and other sleep apnea symptoms.[47] In addition, the severity of the disease was found to be related to adherence rates. Patients with mild OSA (AHI <15) were more likely than severe cases to continue to OA therapy. After a mean of 5 years after the start of OA therapy, 74% of patients with mild OSA were still using their OA, while 50% of patients with severe OSA discontinued OA use.[47] However, discontinuation of treatment in the first year was not related to severity of the disease. Sex, age, smoking habits nor complaints of nasal obstruction were related to poor adherence. Rather feelings of awkwardness when using OA, side effects from treatment or the relief of symptoms were the most commonly cited reasons for poor adherence to OA therapy.[69] These studies relied on surveys and questionnaires to determine patient adherence and did not use objective measures.

1.2.7 Comprehensive model

Human behaviour is complex and is open to multifactorial influences. While some literature tries to pin point what factor is the main determinant of patient adherence, the reality is that this very difficult to predict. Studies that indicated that adherence was influenced by basic factors such as gender, age, psychosocial and socio-economic factors have found that there is a wide variation amongst individuals.[1, 32] Evidence also suggested that patients were often selective in which aspect of their treatment they wish to adhere to.[35] Thus, predicting which patients will be cooperative is very challenging for clinicians. There is no one variable that can be used to predict adherence. The focus needs to shift from predicting patient adherence to developing ways to improve adherence.[18]

A comprehensive model of the determinants for orthodontic adherence was created by Bos et al.[70] Factors that determine patient adherence depend on both the orthodontist/clinician and the patient. The model outlines several intermediary variables, which are fixed factors that cannot be changed, such as gender, age and personality. The antecedent factors can be changed or manipulated, such as pain or discomfort. The consequent factors in orthodontic treatment would be successful or unsuccessful treatment results. With the realization that stable patient variables, such as age, gender and socio-economic status, are poorly related to adherence, the concept now is to focus more on environmental factors that can be manipulated to improve patient behaviour. Techniques that reduce unpleasant side effects, shorten treatment time and use less complex treatment regimens have been shown to enhance adherence. Communication between patient and clinician, influence from parents and family and a patient's own health beliefs can be changed, through cognitive-behavioural approaches, to improve adherence.[18]

Methods to improve adherence was examined by Mehra et al[27] who surveyed 429

orthodontists in the United States of America using an 118-item questionnaire. They found that the best methods of improving patient adherence was verbally praising the patient, educating them on the consequences of poor adherence and discussing treatment goals with the patient. Educating and discussing treatment goals with the parents was also important. Negative methods such as ridiculing the child for poor adherence or increasing fees ranked very low as methods to improve adherence. One of the most compelling findings from this paper was that orthodontists believed that verbally praising patients for cooperative behaviour was the best method to improve adherence. The clinician-patient rapport is very important in successful orthodontic treatment and a strong relationship can help foster more adherent behaviour.

Adherence to treatment for OSA, whether CPAP therapy or OA therapy, may be multifactorial. Gender, age, personality, socio-economic status and cultural differences alone cannot explain whether or not a person will be adherent. Rather, these factors are all interconnected. Many publications have addressed means to increase patient adherence to OSA therapy. Hoy et al[71] found that an active educational program can increase patient motivation, partner involvement and the proactive seeking of solutions to problems. Cognitive behavioural therapy (CBT) programs at an early stage of treatment are very effective if a patient is not adhering to their treatment. It has been found that CBT in conjunction with the standard information package on CPAP increased CPAP usage by 2.9 hours/day over the first month of treatment versus providing the standard information package alone.[13] Shapiro and Shapiro[12] described several practice points to help increase patient adherence. These included educating the patient, including partners and family, about the severity of his or her pathophysiology, encourage the patient to be knowledgeable and involved in his or her treatment plan, focus on good physician-patient communication and plan follow-up appointments with patients. Weaver

et al[13] summarized interventions that improve CPAP adherence. The majority of studies published report on supportive intervention to increase adherence through positive reinforcement. The mechanisms of support varied between studies and included phone calls, print documents and clinical follow-ups. Educational interventions, such as demonstrations, videos and discussions have recently been investigated and it unclear whether these interventions alone influence CPAP or if they influence the mediating variable of interest and knowledge. Further research in this area is warranted. Mixed strategies have also been described which incorporate more than one intervention. Due to the multidimensional nature of adherence, combining various interventions, such as educational and supportive techniques, may help promote greater adherence.[13] For OA therapy, patients experiencing side effects or poor treatment response are likely to withdraw from treatment. Therefore, long-term careful monitoring is essential in this treatment area.[46]

A self-regulation/control theory model has been advocated as an approach to enhance patient adherence. There is evidence that with objective feedback, there is an improvement in patient adherence.[6, 18, 48, 72, 73] Patients are more self-aware and motivated to change their own behaviour when they know that their behaviour is being monitored. This change in behaviour is called the reactive effect of measurement.[18] An example of direct feedback can be seen in electric toothbrushes that record how long a person brushes their teeth. This system was designed to facilitate self-regulation of adherence. This is the basis behind the concept of using microsensors as adherence monitors in OAs. The use of these monitoring devices will provide objective data necessary to make evidenced based clinical recommendations for the prescription of removable orthodontic devices and OAs used for OSA and motivate patients through direct feedback.

1.3 Measurements of adherence in dentistry

Describing a patient's adherence to a prescribed treatment regimen requires clinicians to quantify the degree to which the patient's behaviour coincides with the clinical recommendation.[18] There are several different methodological approaches to measure adherence. The most commonly used method in orthodontics is to rely on clinicians' judgment of patients' adherence. Typical clinical methods for estimating wear-time of devices, such as headgears and removable OAs, include evaluation of patient's oral hygiene, condition of the appliance, such as a worn-looking neck strap, mobility of molars and ease of patient use. Unfortunately, these methods have poor reliability and patients and clinicians tend to overestimate patient adherence.[2, 18, 27, 43, 74] As well, clinicians' judgments are often influenced by therapeutic outcome. This is problematic because it assumes there is a direct link between the clinical outcome and the patient's adherence to the treatment which is not necessarily the case.[18] Sahm et al[7] reported that the ability of an orthodontist to judge patient adherence was at a rate only slightly better than chance.

Another method to monitor to adherence is to rely on patient self-reports. This can be in the form of interviewing patients to report on their adherence to the treatment regimen, questionnaires or asking patients to keep a log record of their adherence. However, asking patients to keep a log does not guarantee that the data is a true representation of their behaviour. Many patients purposefully or honestly misrepresent their behaviour and others do not adhere to the request to keep a written log. Many patients wish to appear more compliant than they actually are in front of their clinician.[18] The retrospective and recall of events, which is required with these methods, increases the overall bias and leads to false representation of the true level adherence.

The role of technology plays an integral part in obtaining objective measures of patient adherence. The idea to incorporate microsensors to monitor adherence is not new. Many investigators have attempted to provide objective adherence monitor and to accurately record details of when patients are wearing their appliances in an effort to provide reliable measures without subjective judgment. The technology to manufacture these microsensors has been improving over the years. A summary of the literature assessing patient adherence using objective monitors is described in Table 1.

1.3.1 Headgear timers

Headgear is a commonly used orthodontic appliance in North America which many patients have a difficult time wearing. The need for an objective measure of headgear adherence has long been investigated. The first headgear timer was described by Northcutt in 1974.[6] The timer, developed by the Aledyne Corporation, consisted of a miniaturized electronic clock made of an E cell circuit that was embedded in the neck strap of a headgear. It worked by simultaneously turning on two switches by the pull of the strap and pressure on the back of the neck while the headgear is worn.[6, 75] The device could also be used in a high-pull headgear.[76] Northcutt reported the accuracy of the timing headgear to be 98.8%.[6] He noted that patients become highly motivated when they are aware they are being monitored and has found a significant increase in patient wear-time since using the device.[75] Similar findings were reported by Mitchell[73] in 1976 at the Ohio State University. He found that in many cases showing no treatment response were starting to make progress as patients were greatly motivated to wear the headgears knowing they were being monitored. As such, the timing headgear demonstrated that was not improper mechanics that was leading to slow treatment progress but rather a lack of

patient cooperation and adherence. Clemmer and Hayes[38] used the Aledyne timers to assess if sex, age, personality and dental attitude were related to adherence. The results indicated that age was not a factor in adherence with headgear wear. However, female patients had higher adherence, as they were more concerned about their dentofacial appearance and attractiveness. Increased adherence was seen in those who had better general attitudes toward orthodontic treatment and perceived their malocclusion as severe. It is important to note that the accuracy of these headgear timers were questioned by Banks,[77] who found that only four of the 13 headgears tested had an accuracy greater than 90%, with the remaining only accurate less than 30% of the time. This indicated that these headgear timers could not provide a consistently dependable recording of actual headgear use.

Many studies have replicated the idea of Northcutt's headgear timer using their own, more consistent, timing devices. In 1991, Cureton et al[78] described how to make a timer using a small ladies' quartz calendar watch and mini lever switch which could be purchased from any local electronic store. They reported an accuracy level of 99.9%. Gurey and Orhan[79], in 1997, described the Selçuk type headgear-timer named after the Selçuk University in Turkey. They reported their quartz watch timer was 100% accurate. The University of Washington created a headgear timer designed to measure temporal headgear wear, estimate the force delivered by the headgear, detect patient attempts to falsify headgear use and provide easily accessible feedback to patients. Through a liquid crystal display (LCD) screen, patients could see their average daily wear-time and/or the cumulative number of hours of wear since their last orthodontic visit in an effort to enhance self-regulation.[74, 80] Cole[4], Doruk et al[81], Agar et al[32] and Brandao et al[48] have measured headgear adherence using a commercially available timing headgear (Compliance Science System, Ortho Kinetics, Vista, California). The device begins monitoring wear when it

is placed under tension and stops when it is released. The device is then placed in an infrared (IR) reader where the data is transferred and stored on computer software. The accuracy of this timing device was found to be 99.6%.[4] Cole[4] compared the objective measures of this timing device to a subjective log of wear-times kept by patients. It was found that 69% of the patients reported their headgear use at an accuracy level of 84% or greater; however, almost one-third, 31%, reported their use at an accuracy level of 58% or less. Doruk et al[81] found that uncooperative patients increased their use of the headgear from four and a half hours to six hours per day when they learned they were being monitored. Similarly, Brandao et al[48] found that patients increase their adherence from 56.7% to 62.7% when they were aware of the recording device. Bos et al[43] developed a headgear timer that recorded temperature (Thermochron i-Button, Maxim Integrated Products, Sunnyvale, California). The timer recorded the headgear as being worn when the temperature was $>30^0$C. It was found that patients and orthodontists overestimate wear-time, mean report time of 11 hours/day and 9 hours/day, respectively. In reality the headgears were only worn for only a mean of 5.58 hours/day.

While orthodontists have long appreciated the value of measuring patients' wear-time of a headgear, the usage of these devices is not mainstream in everyday clinical practice. One of the major problems with these devices are that they are inaccurate,[77] costly[80, 82, 83] and susceptible to patient attempts to falsify headgear wear.[74, 80] Often the timers are bulky and diminish patient comfort when placed in a neck strap.[83] Some designs require the removal of the safety disconnect feature, which is essential for headgear safety, to accommodate the timers.[74, 80] As well, many of the devices only give a cumulative overall measure of wear-time, such that a period of over-adherence just before the next read-out session can make the average wear-time look ideal.[2, 18, 80,

[82] In addition, many of these timers cannot be incorporated into OAs due to their bulky design and incompatibility with the oral environment.

1.3.2 Microsensors for orthodontic oral appliances

The ability to monitor intra-oral appliance adherence amongst patients is even more challenging for orthodontists. The adherence monitors used in extra-oral appliances cannot be used in the oral environment; however, their general principles can be applied to oral devices. One of the first methods used to assess adherence of OA wear was using controlled release glass discs.[82] The controlled-release glass was composed of phosphates, borates and trace elements, which were made into a disc and fitted onto the surface of an orthodontic appliance. The discs would dissolve when in saline solution indicating wear. Problems with this method included the discs coming apart from the appliance due to poor adhesion, surface grinding of the discs would lead to fragmentation and the discs would dissolve at different rates. More recently, Align Technology has incorporated a Blue Dot Indicator into the Invisalign Teen system, which uses the food dye, Erioglaucine disodium salt. The dye is encapsulated in the clear aligner and is released from the polymer in the presence of oral fluid.[84] Manufacturer reported that the embedded dye would dissolve when the exposed to moisture and temperatures equal or higher to body temperature and the clinician can evaluate five potential colour changes (from dark blue to clear) to obtain a graphic representation of the wear-time. This system would allow patients to continually monitor and have instant feedback by checking the colour in the aligners themselves. It is thought that this feedback may be more effective in achieving adherence, especially in older patients.[85] However, Schott and Goz[84] found that the adherence could be easily falsified by patients as the dye would fade when stored in drinking water at 20^0C, which is well below body

temperature. As well, it was found that the dye would fade faster if the aligners were left in the mouth while drinking, stored in water, cleaned with tablets containing oxidizing agents or cleaned in a dishwasher. A large variation in fading was found between patients who strictly adhered to the prescribed wear-times. Due to the fact that the clinicians have to rate the colour change on a five-point scale, this involves inherent subjectivity and does not yield an objective wear-time of the OA.

An objective adherence monitor, much like the ones used in headgear devices, would provide clinicians with a more accurate representation of their patients' adherence of removable OA wear. In 1990, Sahm et al[7, 86] created a reed-switch, which was embedded into a bionator functional appliance and was activated by a magnet system bonded to the lingual of the mandibular first permanent molar. The main problem noted with this device was its bulkiness and patient discomfort. Bartsch et al[2] used the microelectronic timing system developed by Sahm in their study. They found that the actual adherence rate of patients wearing the bionator was only 56.7%.

Currently, there are several microsensors that are commercially available that can be integrated into removable OAs. Scientific Compliance (Atlanta, Ga) invented the Smart Retainer,[87] which is comprised of a miniature microprocessor that can keep time, monitor temperature and store data for up to 40 years. The microsensor records the temperature once every 45 minutes. The data is read off the device by a USB-reader that transmits the data wirelessly through optic signals. This means that only clear appliance material can be used to embed the microsensor to allow transmission of the optic signal. A small short-term randomized clinical trial, funded by Scientific Compliance, was conducted using the Smart Retainers in 19 maxillary Hawley Retainer, worn by subjects 20 hours per day.[72] They reported that individuals

made aware of their wear-time being monitored wore the device significantly more (mean 2.3 hours) per day than unaware patients. Subjects tended to reduce their wear (mean 0.2 hours) with each passing day. In addition, subjects reported to wear their appliances full time but were found to wear the appliances 12.4 hours less than the more honest patients in the study. Thus, from this clinical trial it is evident that there is a significant disparity between the actual and prescribed retainer usage.

The TheraMon sensor (Handelsagentur Gschladt, Hargelsberg, Austria)[83, 88] was developed at the same time as the Smart Retainer in Europe. It works by recording temperature of the oral environment at 15-minute intervals. Temperatures noted between 31.5^0C and 38.5^0C are recorded as wear-time. The company reports that sensitivity of the temperature module makes it very difficult for patients to fake adherence as the software highlights any abnormal temperature fluctuations as "suspicious" activity. The microsensors transmit data though a radio frequency identification device (RFID) and do not emit any frequency except when communicating with the reader.[88] In vivo testing of the microsensor was conducted by Schott and Goz[83] on 20 patients fitted with upper and lower active plates, functional appliances or retention devices. However, the paper only provides a case report of one patient wearing an upper appliance and does not provide any statistical analysis on the accuracy of the device. More recently, in October 2013, Schott et al[44] published a study examining the adherence rate of 100 patients fitted with Hawley retainers or functional appliances during the retention phase of their orthodontic treatment. While patients were instructed to wear the appliances a minimum of eight hours per day, it was found that during the first three months, 60% of patients wore the retainer for a mean of less than 8 hours/day, 25% wore it between 8-10 hours/day and 15% wore it more than 10 hours/day. The median wear-time was 7.0 hours/day. While the report stated that

adherence rates were influenced by age, sex and place of treatment, these differences were not statistically significant. However, patients receiving government funded statutory health insurance wore their appliances significantly more than patients with private insurance. This is the first study to examine the association between clinical and social parameters and report objective wear-times of removable retainers using an incorporated microsensor.

In November 2013, Pauls et al[89] used TheraMon microsensors in a 168-day trial where a control group of 14 patients fitted with removable appliances were told about an adherence monitor embedded in their appliance. A study group of 18 patients were not told about the adherence monitor until after the first appointment. It was found that the subjective reports of adherence significantly differed from the objective measured adherence at the first appointment when the study group did not know they were being monitored. However, subsequent to being told of the monitoring device, there was no significant difference in reported usage compared to the recorded use at later appointment. Thus, patients tend to overestimate their wear-times but become more realistic and honest once they know they are being monitored. In addition, it was found that there was no significant difference in the wear-time between the two groups. This suggests that adherence does not necessarily increase when patients know they are being monitored.

The TheraMon microsensor has been used in several clinical studies[15,44, 89]; however, investigation on the microsensors accuracy has not been thoroughly investigated. Schott and Goz[90] attempted to assess the accuracy of the Smart Retainer compared to the TheraMon microsensor by *in vitro* testing using a programmable water bath. They reported that the TheraMon microsensor was more accurate, with the Smart Retainer overestimating wear-time by one hour. Pauls et al[89] cited this study as evidence that clinically sufficient accuracy of the

TheraMon sensor has been investigated *in vitro.* However there are several flaws to this study including an unreported sample size, no statistical analysis and programming a water bath to room temperature and oral temperature while not taking into account the time it takes for the water bath to heat or cool. Pauls et al[89] attempted to show accuracy of the TheraMon microsensor *in vivo* by having a postgraduate student wear a removable appliance with a microsensor for 2 weeks and record when the appliance was inserted and removed. It was found that there was a mean discrepancy of 7.92 minutes per day between the wear-time recorded by the microsensor and the log kept by the student. The level of evidence on the microsensor's accuracy is quite low as the sample size was only one and the trial was over a short period of time. In addition, no statistical analysis was provided.

1.4 Measurements of adherence in sleep medicine

The earliest studies published on adherence to both CPAP therapy and OA therapy relied on self-reports, including diaries and verbal recall. This is similar in dentistry, where clinicians were forced to rely on subjective measures to describe patient compliance. CPAP therapy is regarded as being successful if the patient's apnea hypopnea index (AHI) drops below five when the CPAP is used. Approximately 15-30% of patients with OSA refuse CPAP therapy and 20-40% will discontinue CPAP after three months.[91] Current trends define adherence with CPAP therapy to be usage for 4 hours/night in 70% of nights.[11, 91] Pooled data, from a review article by Hoffstein, which summarized 21 reviewed studies on OAs for OSA involving 3,107 patients, showed that at the end of 33 months, only 56–68% of patients continued to wear their OAs. However, there is wide variability between individual investigations. Adherence rate range from as little as 4% to as high as 76% at the end of 1 year.[92] It is also important to note that the

majority of these studies relied on subjective measures of compliance, including questionnaires and interview, which may mean that actual adherence rates were much lower.

1.4.1 CPAP adherence monitors

Technological advances in manufacturing CPAP devices have created adherence monitors that do not merely measure the hours the machine is on but they can also record the duration that the mask is on at an effective pressure level. It has been found that there is a 10% difference between machine-on recorded adherence and mask-on adherence.[20] Reeves-Hoche et al[10] described a 5-volt electric elapsed hour monitor that was covertly inserted in CPAP machines that was capable of recording when the unit were operating and included a pressure sensor switch. Therefore, if there was a large leak or if the patients failed to wear the mask but the unit was turned on, the pressure monitor would switch off. From a sample of 47 patients with OSA, they found that 9 subjects discontinued therapy within 3 months for various reasons. The remaining subjects had an average nightly use of 4.7 hours, which was 68% of total sleep time of the patients. It was also found that AHI did not correlate with adherence and no predictors of adherence were found.

Rauscher et al[9] investigated self-reported measures of adherence through questionnaires compared to objective built-in adherence monitors in CPAP units. The study involved 63 consecutively treated patients with OSA. The mean measured used time was 4.9 hours per night. The reported daily usage was overestimated at a mean of 6.1 hours per night. The mean reported time in bed sleeping was 7.7 hours a night with the CPAP used 90% of the time in bed. However, it was found with the adherence monitor that the CPAP was only used for 64.3% of the time spent in bed. Thus, from this study, one can conclude that self-reports are an inaccurate tool to

determine patient adherence. Trying to estimate nightly wear through questionnaires, interviews and self-reports tend to overestimate the actual time and should be used with caution.

1.4.2 Microsensors for oral appliances for obstructive sleep apnea

Oral appliances used for the treatment of OSA, such as mandibular advancement devices (MADs), , present similar issues of patient adherence as orthodontic appliances. A summary of literature that has examined patient adherence to OA therapy using objective adherence monitors is described in Table 1. Lowe et al[14] published the first report using a microsensor embedded into an OA for sleep apnea in 2000. They fabricated an adherence monitor using a ceramic thick-film hybrid with a memory system, which would monitor wear-time based on temperatures above 31^0C. The OA were tested over a two-week time span in eight patients with OSA. The index of agreement between the subjects' adherence monitor and log records was 0.99. However, Lowe et al[14] reported several problems with the monitors such as the damaging effect of saliva, heat intolerance of the electronic components and energy consumption over a long period of trial time.

Tjin et al[93] described the use of fibre-optic sensors to monitor the force and temperature of OAs worn by patients suffering from sleep apnea. Using Fibre Bragg gratings fabricated from photosensitive fibres, the sensors can monitor temperature changes of 0.1^0C and detect forces of 0.5N. The main advantage of these sensors is their small size (1 cm long by 3 mm wide and 0.375 mm thick) and immunity to electromagnetic interference. However, a detailed study of the accuracy of the sensors has not been published.

Inoko et al[94] examined the cytotoxic effect of a "temperature data logger" (Thermochron iButton, Dallas, Texas) through in vitro testing using a three-dimensional human dermal model

kit, which was derived from human normal keratinocytes and fibroblasts. Due to the fact that the sensor is covered with stainless steel alloys, the investigators were concerned that the sensor may corrode in the oral environment and the corroded material would be in direct contact with periodontal tissues. The results indicated that the sensor immersed in the human dermal tissue kit for 10 days had a minimal cytotoxic effect, as the cell viability of the extracted fluid was 96.92%. The study concluded that the sensors were not influenced by oral moisture and could be an effective and safe method for measuring OA adherence. In the second part the Inoko et al[94] study, six patients with OSA were fitted with an OA with the Thermochron sensor attached to the buccal surface and were instructed to wear the appliance for one month. They reported that all participants wore the appliances every day, except one who wore it only 20% of the time. The average time used ranged from 5.4 to 7.5 hours per day. No statistical analyses were done to evaluate the results. The sensor used was quite large with a diameter of 17.4mm, thickness of 5.9mm and weight of 3.3g. The use of this large sensor in everyday clinical practice may be challenging for some patients. The results of an abstract, testing the same thermosensitive microsensor (Thermochron iButton) embedded into an oral elastic mandibular advancement device in seven patients with OSA, found that the devices were worn approximately 90% of days in the trial for a mean of approximately 6.2 hours per day. The study concluded that adherence to MADs could be objectively assessed with temperature microsensors.[95]

The first trial using TheraMon microsensors (Hargelsberg, Austria) as an adherence monitor in OAs was a three-month prospective clinical trial followed 51 consecutive patients who were previously diagnosed with sleep-disordered breathing (SDB). The microsensors were embedded into the upper right side of a custom-made titratable MAD. The results found regular OA user rate was 82% with an average objective OA use of 6.7±1.3 hours per day. There was no

significant difference between the computed objective data from the microsensors and self-reported log of OA adherence. The study proposed and was able to calculate the mean disease alleviation as a measure of therapeutic OA effectiveness, where effectiveness has to entail both efficacy and adherence. The mean disease alleviation can be calculated as the surface area on a graph by multiplying the adjusted adherence rate (objective OA usage divide by total sleep time) and the therapeutic efficacy (AHI at baseline minus AHI with OA applied). It was found that OA therapy has a mean disease alleviation of 51.1%, which is comparable to the 50% adjusted CPAP effectiveness[96]. The values of the mean disease alleviation of CPAP are then similar to OA therapy, where OA has a high adherence rate with suboptimal efficacy, and CPAP therapy has higher efficacy but decreased adherence. Still, the proposed mean disease alleviation calculation needs to be further studied to understand if it truly correlates with clinical outcomes. In this same study, no adverse effects, including oral burns, lesions or detachment of the microsensor, were reported by the participants. Only one sensor was disqualified due to technical problems. While there are several limitations to this study including relatively small sample size, short follow up period and no control group, this study provides an excellent foundation to create clinical guidelines using evidence based research using objective thermosensitive microsensors.

AIR AID SLEEP (AIR AID GmbH & Co KG, Frankfurt, Germany) microsensors were adapted from the TheraMon microsensors to be used more specifically for the demands of dental sleep medicine. While the microsensor's program is based on the software used by TheraMon, there are several differences between the sensors. TheraMon software requires a lab technician to activate the microsensors before giving the sensors to the clinician/orthodontist. The AIR AID SLEEP software combines the software to allow the clinician to decide when to activate the sensor. One of the most important objectives in the development of this sensor was to compare

adherence measurement with CPAP. Therefore, the frequency of temperature recording was shortened to an interval of five minutes compared to the 15-minute interval used by TheraMon. The AIR AID SLEEP stores data for only 33 days of wearing time, which is significantly shorter than the 100 days of data stored on the TheraMon. This is a big disadvantage for patients who will have to return for appointments once a month to have the device read-out by the clinician.

DentiTrac is a new microsensor developed by BRAEBON Medical Corporation (Kanata, Ontario). The microsensor is currently undergoing beta testing. The DentiTrac is a thermosensitive microrecorder that records temperatures between 33.5-39.2^{0}C as wear-time. DentiTrac records temperature at a sampling interval of five minutes, similar to the AIR AID SLEEP microsensors. Reading the data off from the sensors is done via infrared and takes one minute to load the data regardless of how long it has been since the last reading. DentiTrac has a base reading station for both the clinician and the patient. This allows to patient to monitor their own adherence and upload their data remotely. Similar to the TheraMon and AIR AID SLEEP microsensors, the DentiTrac has anti-deception detection. However, the software is more sophisticated than the others, as the microsensors will only record when in the mouth. They will not record any wear-time while in a water bath according to the manufacturer. TheraMon and AIR AID SLEEP will only alert to suspicious activity when the sensors are in a water bath but will still record this time as wear-time. The DentiTrac has a storage capacity of 180 days, which is longer than the TheraMon and AIR AID SLEEP but less than the Smart Retainer. The main factor that differentiates this sensor from the others available is that it records head movement and head positioning through the use of a three-axis accelerometer. This information may be useful in the investigating OAs for OSA as clinicians and researchers need to be sure that the appliance is being worn when the patient is sleeping, indicated by a supine head position. The

recording of head movement also allows clinicians and researchers to have a better understanding of how the person sleeps although head position and body position correlations have not been assessed.

Table 1. Summary of evidence of microsensor adherence monitors

Device	Sample size (n)	Conclusion on adherence	Reference
Headgear	N/A	Introduced first headgear timer. Timing headgear was 98.8% accurate	Northcutt, M.E (1974)[6, 75, 76]
	>200	Patients increase headgear wear from 35-50 hours/week to over 100 hours/week when they were aware of monitor	Northcutt, M.E (1975)[75]
	N/A	Timer can also be used in high pull headgears	Northcutt, M.E (1976)[76]
	N/A	Editorial paper commenting on how adherence increases with the headgear timer and how wear-time is no longer subjective.	Mitchell, J.I. (1976)[73]
	13	In vitro testing: Only 4 timers showed accuracy above 90%. The remaining 9 timers showed accuracy below 30%.	Banks, P.A & Read, M.J. (1987)[77]
	N/A	Headgear timer made from ladies' quartz calendar watch is 99% accurate	Cureton, S.L. et al (1991)[78]
	28	Orthodontists, residents, and assistants overestimate patients headgear wear 60%, 71%, and 73% of the time. Orthodontists, residents, and assistants underestimate headgear wear 40%, 29%, and 27% of the time.	Cureton, S.L. et al (1993)[5, 42, 78]
	10	Headgear timer was 100% accurate Patients who knew they were being monitored increased wearing time by 26% (from 10 to 14 hours/day)	Guray, E. & Orhan, M. (1997)[79]
	N/A	Discussion on self-regulation model of patient adherence and description of prototype headgear monitor	Lyons, E.K & Ramsay, D.S. (2000)[74, 80]
	N/A	Laboratory testing of headgear monitor; headgear timer is 99.999% accurate	Lyons, E.K & Ramsay, D.S. (2002)[80]
	20	69% of patients reported headgear use at an accuracy level of 84% or higher; 31% reported use at an accuracy level of 58% or lower.	Cole, W.A. (2002)[4]
	46	80% of uncooperative patients increased their headgear use by 4.5-6 hours when they knew they were being monitored.	Doruk, C. et al (2004)[81]

Device	Sample size (n)	Conclusion on adherence	Reference
Headgear	51	Headgear adherence not related to age, gender, or psycho-social factors	Agar, U. et al (2005)[32]
	21	Patients wore headgear only 56.7% of prescribed hours. This increased to 62.7% when they knew they were being monitored	Brandao, M. et al (2006)[48]
	56	Mean headgear wear-time was 5.58 hours. Subjective measures overestimate wear-time. Patients, parents, and orthodontists overestimate headgear adherence	Bos, A. et al (2007)[43]
Intra-oral appliances	?	Preliminary trials of soluble controlled-release glass timing discs indicate that they can give a simple, economic, and reasonably accurate method of assessing patient adherence.	Savage, M. (1982)[82]
	53	Mean adherence rate was 50.59%, mean recorded hours of daily wear was 7.65 hours (out of 14.9 hours of required wear)	Sahm, A. et al (1990)[75]
	53	Reliability of patient reports of adherence depend on how detailed the clinician questions were and whether the clinicians draws his/her own conclusions from the information received instead of leaving them to the patient.	Sahm, A. et al (1990)[7, 86]
	77	Actual rate of adherence averaged 56.7%, 8.7 hours/day; adherence was related to family background, conformity, and degree of parental supervision. Treatment duration, dominance of provider, and interpersonal perception are interdependent and/or consequent variables.	Bartsch, A. et al (1993)[2]
	14	Evaluation of adherence indicators, food-grade dye embedded in clear aligners: colour changes recorded for the adherence indicators correlated with the number of hours of wear recorded by the patients. Stronger correlation was found for males than females.	Tuncay, O.C. et al (2009)[85]
	N/A	Description of Smart Retainer microsensor	Ackerman, M. et al (2009)[87]

Device	Sample size (n)	Conclusion on adherence	Reference
Intra-oral appliances	19	Subjects who were made of aware of the monitor wore the appliance 2.3 hours longer than those unaware. Subjects reduced appliance wear by 0.2 hours each day. Subjects reporting full usage of the appliance wore it 4.3 hours more than those reporting less than full usage. Subjects who misrepresented their appliance use wore it 12.4 hours less than the more honest subjects.	Ackerman, M. & Thornton, B. (2011)[72, 87]
	2?	*In vitro* comparison of Smart Retainer and TheraMon microsensors: both microsensors can be used as an objective wear-time monitor in orthodontic appliances. The smaller TheraMon offers greater versatility and analysis of wear-time.	Schott, T.C. & Goz, G. (2010)[90]
	20	20 patients tested but only 1 case report presented. The objective measure of wear-time may lead to a paradigm shift in how to prescribe wearing times of orthodontic appliances.	Schott, T.C. & Goz, G. (2011)[83]
	N/A	Description of TheraMon microsensor	Schott, el. al (2011)[88]
	21	*In vitro* testing of adherence indicators in clear aligners demonstrate that colour fading occurs as a function of time, pH, and temperature when the stored in drinking water, soft drinks, cleaning tablets, and/or dishwashers. The indicators can be easily manipulated.	Schott, T.C. & Goz, G. (2011)[84]
	100	TheraMon microsensors were embedded into Hawley retainers and removable functional appliances during the retention phase of patients' orthodontic treatment (3 months). Median wear-time was 7.0 hours/day. 60% of patients wore the retainer for a mean of less than 8 hours/day, 25% wore it between 8-10 hours/day and 15% wore it more than 10 hours/day. There was no statistical significant difference between appliance type, age, gender or treatment center. Patients with government health insurance wore appliances significantly more than patients with private insurance.	Schotts, T.C. et al (2013)[44]

Device	Sample size (n)	Conclusion on adherence	Reference
Intra-oral appliances	32	TheraMon microsensors were embedded into removable appliances over 168-day period. Subjective reports of wear-time significantly differed from objective measures when subjects did not know they were being monitored. There was no significant difference in subjective reporting when subjects knew they were being monitored. Knowing they were being monitored did not increase wear-time of appliance.	Pauls, A. et al (2013)[89]
OAs for OSA	8	OA was worn for a mean of 6.8 hours per night	Lowe, A.A. et al (2000)[14]
	?	*In vitro* testing of FBG sensors in dental splints for OSA - monitoring of both the pressure and temperature of the dental splint can give a clear indication of patient adherence.	Tjin, S.C. et al (2001)[93]
	6	*In vitro* testing showed minimal cytotoxic effects of the microsensor. During in vivo testing, 2 patients wore the OA every day, 1 patient only used it 20% of the days. No negative results with the sensor were reported.	Inoko, Y. et al (2009)[94]
	7	OA was worn for 90.1±12.2% of days. The mean average daily use on days used was 6.2±1.2 hours	Abrams, E., et al (2012)[95]
	51	OA, with embedded TheraMon microsensors, were used 6.7±1.3 hours/day. The adherence of days/week was 91.2±10.1%. The rate of regular OA users was 82%. Mean disease alleviation was 51.1%	Vanderveken, O.M., et al (2013)[15]

N/A- Not applicable, ?- Not reported

1.5 Study Rationale

Previous studies examining patient adherence have suggested that at least 25-50% of the general population fail to comply with all aspects of their medical treatment. Non-adherence rates may be as high as 80%.[3] One of the key gaps in research of OSA, as outlined by Agency for Healthcare Research and Quality in 2012,[97] is that there are no studies that have evaluated the predictors of adherence with OAs and that trials addressing adherence have only been objectively done for CPAP treatment. A small microsensor that can be embedded into an OA would allow for direct comparison of adherence with different interventions and for incorporation of adherence into an overall comparison of effective treatment. A well-designed randomized control trial study to evaluate the effectiveness of OAs needs to use established metrics to measure adherence. Thus, it is important to examine the accuracy in the recording capabilities of the microsensors on the market in order to determine if these microsensors can be used for research and clinical purposes.

Clinical simulation bench work has not been done to compare these adherence monitors. As well, there are no bench studies evaluating if the different materials used in appliances would influence their accuracy. To date, there are no peer-reviewed published studies that have evaluated the accuracy of the DentiTrac microsensor or their use in a clinical setting. With the DentiTrac microsensor being manufactured in Canada and beginning to become commercially available to clinicians in North America, it is important for an independent investigator to evaluate their accuracy. This information will be critical for clinicians to decide whether or not they wish to incorporate such microsensors into their treatment. In addition, there are no studies that have assessed the accuracy of these microsensors in *in vivo* testing. With recent literature[15, 44, 89] now being published using these microsensors as a means to objectively measure adherence,

it is important to investigate their accuracy to ensure validity of their results discussed in the literature. The three main adherence monitors, which are most likely to be used in the near future, were then selected to be studied. A summary of their characteristics is described in Table 2.

Table 2. Comparison of TheraMon, AIR AID SLEEP and DentiTrac microsensors

	TheraMon (Sensor T)	**AIR AID SLEEP (Sensor A)**	**DentiTrac (Sensor D)**
Dimensions (mm)	12 x 8 x 4.5	12 x 8 x 4.5	10.5 x 8.5 x 4
Weight (g)	0.4	0.4	0.5
Read out procedure	Radio frequency identification device (RFID)	Radio frequency identification device (RFID)	Infrared (IR)
Temperature range (^{0}C)	-25 to 60	-25 to 60	33.5-39.2
"Wear" Temperature range (^{0}C)	31.5-38.5	31.5-38.5	33.5-39.2
Temperature sensitivity (^{0}C)	0.1	0.1	0.1
Sampling interval (min)	15	5	5
Software	PC	PC	Cloud/ PC
Delivery	Shipped out in "sleep mode", activated by lab technician when ready to use. (Can last 1 year in "sleep mode")	Shipped out in "sleep mode", activated by clinician when ready to use	Installed by certified labs who provide full verification of operation before delivery to the dentist
Memory capacity	16 kb	16 kb	
Storage capacity	100 days	33 days	180 days
Head position	N/A	N/A	Supine/non supine
Head movement	N/A	N/A	YES
Anti-deception detection	YES	YES	YES
Clinical base station	YES	YES	YES
Patient reader station	N/A	N/A	YES
Download time (min)	≥ 1	≥ 1	1
Battery life	> 18 months with 96 hour recharge	> 18 months with 96 hour recharge	> 24 months
Insertion into appliance	Completely embedded in acrylic	Completely embedded in acrylic	Completely embedded in acrylic

The objective of this study was to evaluate the accuracy of microsensors, which can be embedded into OAs and used over a long-term period in the oral environment. The hypothesis for this study was that the computed wear-time readings from the microsensors are similar to recorded log times. This would demonstrate that an objective method could be used to quantify adherence of removable OA and OAs used for OSA. The null hypotheses were:

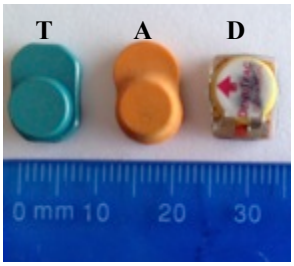
1. There is no difference in the recorded log times and the computed log of the microsensors *in vitro* and *in vivo* testing
2. There is no difference between the different microsensors types in *in vitro* and *in vivo* testing
3. There is no difference in performance with different durations/intervals of wear-times
4. There is no difference in the recorded log time and computed readouts when the microsensors are embedded in different types of material

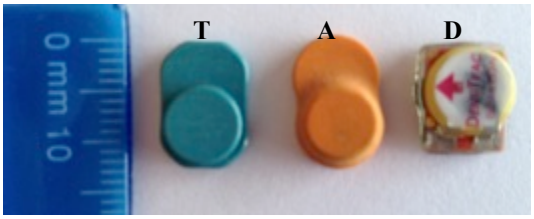
Chapter 2: Methods

The prospective study was designed to assess the reliability of microsensors to detect temperatures similar to the range found in the oral cavity, 34-37 ^{0}C.[98-101] Phase 1 of this research project involved *in vitro* laboratory testing. The method of this study is based on the research of Schott and Goz[90] who found that a water bath could be used to replicate the oral environment. Phase 2 consisted of *in vivo* testing of the microsensors embedded into appliances and worn by volunteers.

The three tested microsensors and their respective read-out stations used in phase 1 were: Sensor T (TheraMon), Sensor A (AIR AID SLEEP) and Sensor D (DentiTrac), shown in Figure 1 and Figure 2. See Table 2 for technical specifications of the microsensors. Sensor T and Sensor A are comprised of a microelectronic chip with an application specific integrated circuit with an Electronically Erasable Programmable Read-Only Memory (EEPROM). The microsensors contain a thermal sensor, quartz oscillator and a 3.0 Volts Li-dry-cell accumulator. Sensor D is micro-recorder containing a microprocessor with 12-bit analog to digital converter (ADC), 3-axis accelerometer, thermistor and external memory. It is powered by a very small lithium battery.

Figure 1. Width and height of the three microsensors





Sensor T = TheraMon
Sensor A = AIR AID SLEEP
Sensor D = DentiTrac

Figure 2. Read out stations for the three microsensors

Sensor T Reader **Sensor A Reader** **Sensor D Reader**

Phase 1, *in vitro* testing, was done to assess the reliability of the three microsensors in a laboratory setting. Two thermostatic water baths (Whip Mix Digital Water Bath, Farmington, Kentucky), filled with approximately 1 L of water, were programmed to 35 ^{0}C, as shown in Figure 3. The water baths were preheated for at least one hour to the desired temperature prior to insertion of the microsensors, to ensure the bath were at a stable desired temperature without fluctuations. Aluminum foil was used to cover the water to prevent evaporation and temperature fluctuations. Temperature was confirmed using a mercury thermometer. It was noted that the temperature in the water bath fluctuated up and down 2 ^{0}C throughout the trial. This is acceptable as the temperature still falls within the range found in the oral cavity.[98-101] A log sheet was kept to record exactly when the microsensors were placed into and removed from the water bath. The same timer was used throughout the experiment. No effort was made to keep the microsensors in the same location or orientation in the water bath throughout the trials.

Figure 3. Whip Mix digital water bath

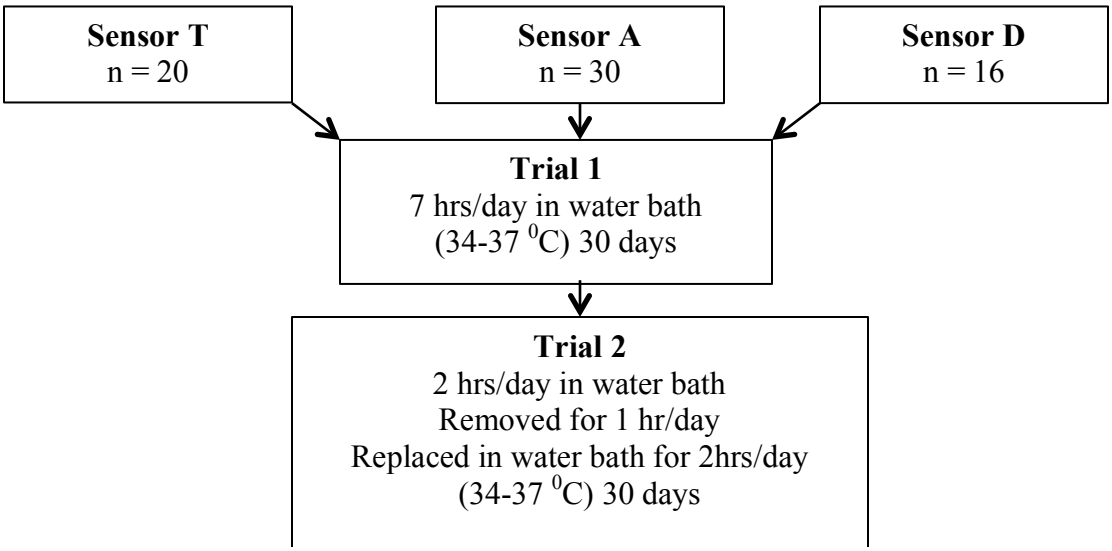
2.1.1 Phase 1, Trial 1

The first trial, called long duration interval, consisted of placing the microsensors (Sensor T, n = 20; Sensor A, n = 30; Sensor D, n = 16) in the water bath continuously for seven hours per day for 30 days. The sensors were out of the water bath for 17 hours of the day. This duration was chosen to simulate long term durations of wear, such as nighttime wear during sleep. (See below, Figure 4, for schematic of the study design.)

2.1.2 Phase 1, Trial 2

In the second trial, called short duration interval, the same microsensors used in Trial 1 (Sensor T, n = 20; Sensor A, n = 30; Sensor D, n = 16) were placed in the water bath for 2 hours, removed from the water for 1 hour and replaced into the water for 2 more hours each day, for a total of 30 days. This resulted in the sensors being placed in water for a total of four hours and out of the water for 20 hours each day. The pattern was used to simulate daytime wear when patients remove and replace their appliances before, during and after mealtimes. (See below, Figure 4, for schematic of the study design.)

Figure 4. Schematic of phase 1, trial 1 and 2, study design



2.1.3 Phase 1, Trial 3

The third *in vitro* trial tested the effects of different OA material on the microsensors ability to record temperature. Sensor T (n = 9), Sensor A (n = 9) and Sensor D (n = 9) were embedded into three different materials: acrylic, polyvinylchloride (PVC) (Essix, 0.035" thick) and thermoactive acrylic (Veriflex), with n = 3 for each sensor in each material. Blocks of standard thickness were made by an orthodontic laboratory technician (Space Maintainers Laboratories, Vancouver, British Columbia) (Figure 5). The blocks with the embedded sensors were placed into the water bath for seven hours continuous per day for 30 days. The blocks were kept out of the water bath for 17 hours each day. (See Figure 6 for schematic of trial 3 study design.)

Figure 5. Example of the microsensors embedded in blocks of material

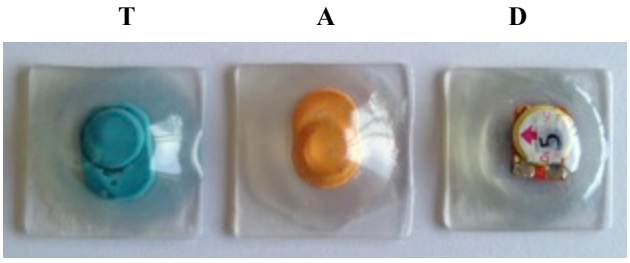
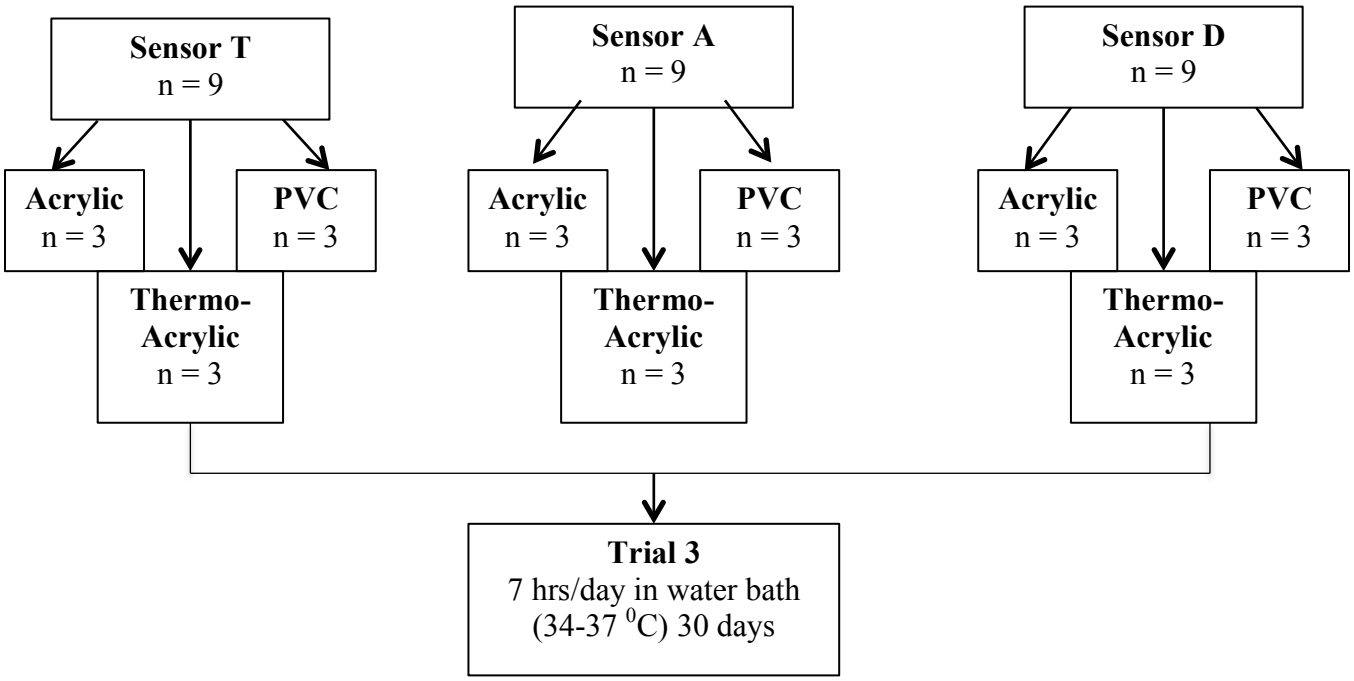


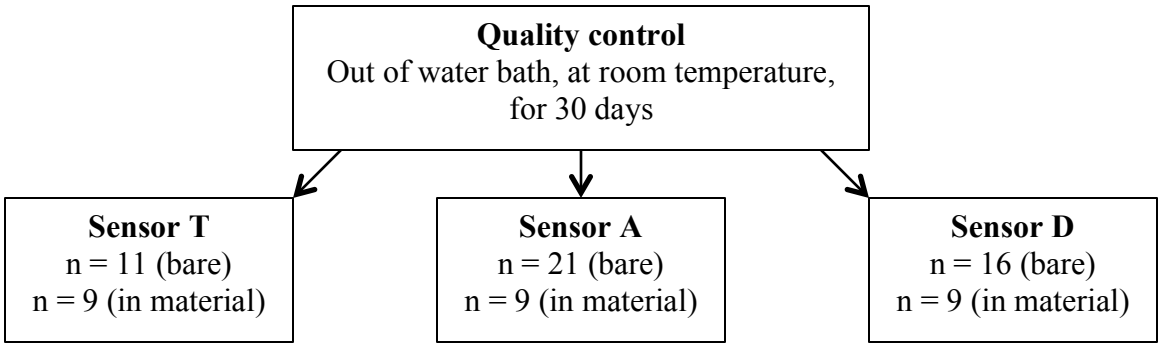
Figure 6. Schematic of phase 1, trial 3 study design



2.1.4 Quality control

The microsensors were left out of the water bath for 30 days to see if they recorded any "wear-time". This was used to determine if there were any false positive readings from the microsensors. While the microsensors were not being used, they were stored in a plastic container at room temperature. They were kept in a dry area away from any sunlight. (See Figure 7 for schematic of control trial study design.)

Figure 7. Schematic of quality control trial



2.2 Phase 2: *In vivo testing*

Phase 2 consisted of *in vivo* testing of the microsensors. Ethics approval was granted by the Clinical Research Ethics Board at the University of British Columbia (H12-00855). Fourteen volunteers, six females and eight males, were recruited from the student population base at The University of British Columbia, Faculty of Dentistry. Informed consent was obtained from all the participants (Appendix A). To standardize the appliance design, the exclusion criteria included participants with missing teeth (except wisdom teeth), any orthodontic appliance currently being worn by a participant (except fixed lingual retainer wires), active periodontal disease, any type of oral pathology (including caries, cleft lip and palate) or a history of claustrophobia or difficulty wearing dental appliances. Maxillary impressions, using alginate (Kromopan 1000), were taken of the participants and were poured up in dental stone. Vacuum formed retainers (Essix, 0.035'') were fabricated for each participant. One Sensor D was attached to the right buccal surface of retainer and one Sensor A to the left buccal surface using acrylic, as illustrated in Figure 8. The appliances were fitted intraorally in the participants to ensure accurate fit and comfort. Participants were instructed to wear the appliance at night, while sleeping, for 30 days. Participants were given a log, attached in Appendix B, to record the time of day, to the minute, that they inserted the appliance at night and removed it in the morning. Participants brought in their appliances to have the data read out after day-15, to ensure they were recording, and then again after day-30. The appliances were pretested and post-tested in a water bath, for seven hours for one day, to ensure the sensors were working throughout the *in vivo* testing. Only data from sensors with accurate pre- and post-test measures were included in the study. (See schematic of the study design in Figure 9.) Participants were also given a questionnaire regarding demographic, sleep history questions and concerns regarding discomfort (Appendix C).

Figure 8. Example of vacuum formed retainer with embedded microsensors

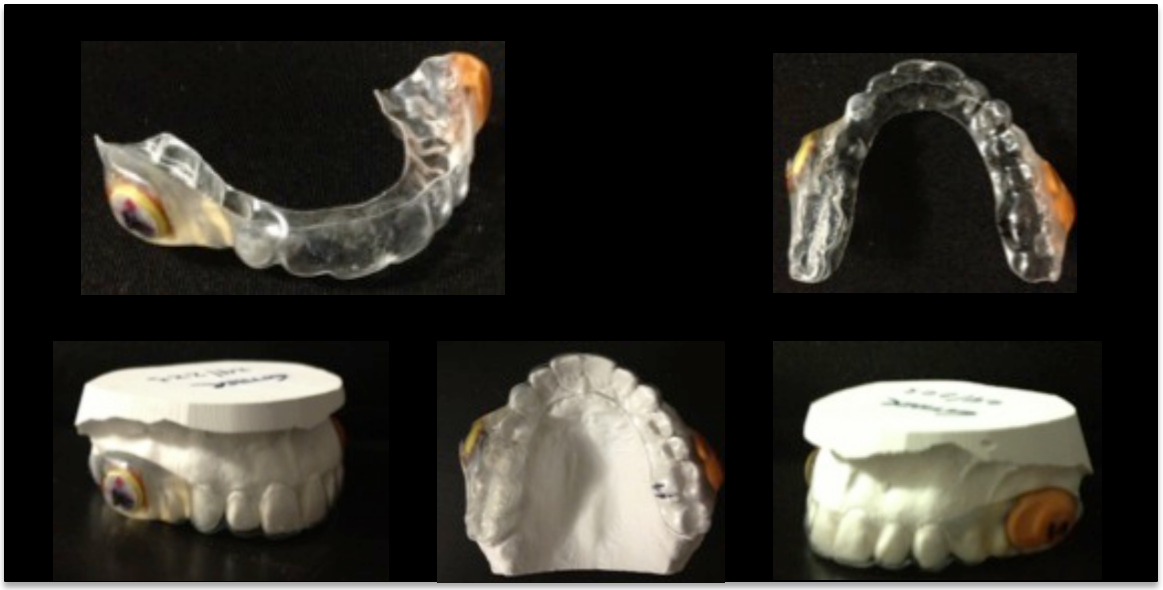
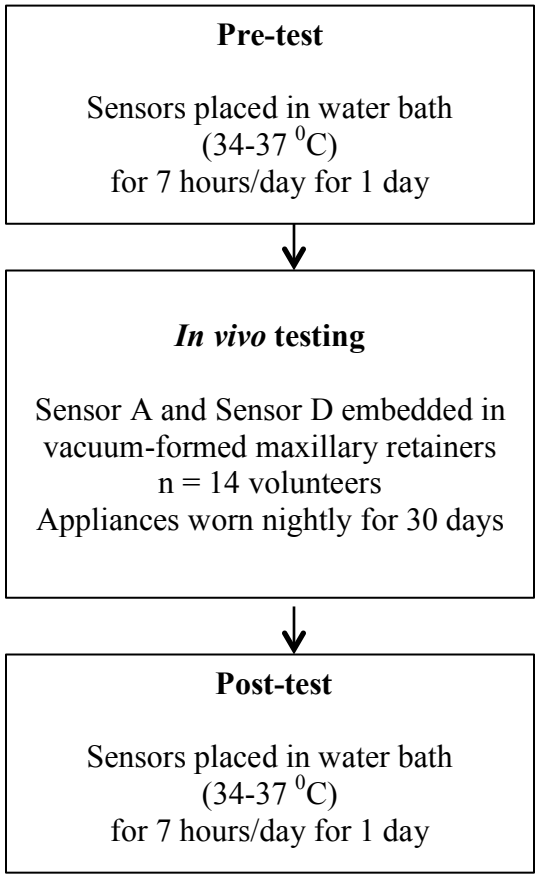


Figure 9. Schematic of Phase 2 study design



2.3 Data Analysis

2.3.1 Phase 1: In vitro *testing*

Raw data was exported from the software of the three microsensors. Sensor T and Sensor A raw data included date, time and temperature (^{0}C). Sensor T records temperature once every 15 minutes and Sensor A records temperature once every 5 minutes. All temperatures recorded in the range of 31.5-38.5 ^{0}C were designated to represent "wear-time". Sensor D raw data includes date, time, temperature (^{0}C), head position, head movement, process head position, wearing and wearing with head position lying down. Only date, time and temperature were analyzed for the purpose of this study. Sensor D records temperature once every 5 minutes. Only temperatures between 33.5-39.2 ^{0}C are recorded and designated as "wear-time". To calculate the "wear-time" for each microsensor, the number of temperature recordings that were found within the microsensors' temperature range was multiplied by the recording interval (i.e. 5 or 15 minutes, depending on the microsensor type). Data was subsetted by temperature and experiment date. All of the times the temperature fell within the specific range for a given experimental day were aggregated and summed, so the final data set for analysis had one row per sensor-day.

It was considered that the paper logs were accurate. Each sensor time was subtracted from the corresponding logged time to obtain the response difference in minutes. Absolute values of the deviation were then obtained and recorded as absolute response difference. In the statistical analysis of the results, the absolute response difference results were used. Frequency of over- and under-estimates was assessed based on the response difference results.

Scatter plots were made for the response difference data to illustrate how much microsensors deviated from the logged time for each trial. Twice the sensing interval (+10 minutes and -10 minutes for Sensor A and D, +30 minutes and -30 minutes for Sensor T) was

used as acceptable thresholds for the deviations to fall within. Red lines on the scatter plots indicate the thresholds. These scatter plots provide a visual of the over- and under-estimations of the microsensors' responses and outliers can be easily seen.

Scatter plots for the absolute response difference were made with the outliers removed. The blue lines on these graphs indicate the median absolute deviation for the sensors in that trial and the red line indicates twice the sensing interval threshold.

2.3.2 Phase 2: In vivo *testing*

The computed read out data from the microsensors were collected from the graphs that the Sensor A and Sensor D software produced, rather than exporting the raw data. Thus, all factors of the microsensors algorithm to determine "wear-time" (including head movement for Sensor D) were taken into account during the data analysis in this phase. The response differences and absolute response differences are summarized as scatter plots.

2.4 Statistical Analysis

Three different microsensor types were used to record OA "wear-time" while submerged in a water bath. The primary factor of interest was the *Sensor* type and it had three levels (A, T and D). The response variable was the difference in time, calculated by the computed temperature time minus the logged time for each day of the experiment. The absolute values of the response differences were used for statistical analysis. Univariate ANOVA was conducted for each trial in Phase 1 and Phase 2 to see if there were any statistical differences between the microsensor types. Post hoc Scheffé multiple mean comparison was used to determine where the

differences lied. The statistical analysis of the results was conducted using IBM SPSS Statistics 21.

Chapter 3: Results

3.1 Phase 1: *In vitro* testing

No technical problems were found with Sensor A and T microsensors; therefore, all of Sensor A and Sensor T were included in the statistical analysis for all 3 trials of phase 1 testing. Three out of 25 Sensor D were faulty. Sensor D 317 was missing proper readings intermittently in January 2013. That microsensor only recorded "wear-time" temperatures on 42 of the 60 experimental days. In addition, Sensor D 317 had several days in January 2013 where 3 or 4 extra hours were recorded. It was noted upon reading of Sensor D 317 in early January 2013 that the microsensor was already recording for dates that had not yet occurred in the calendar. It is not clear what happened to this microsensor's internal clock. This microsensor was removed from the analysis. In addition, Sensor D 323 only recorded "wear-time" temperatures on 21 of the 60 days, suggesting problems with the sensor's battery. In sensor D 301, which was embedded in acrylic material, the battery died prematurely and only 15 of the 30 days were recorded. Only the days that recorded data were included in the analyses. With the faulty microsensors and days removed, there was a total of 4770 observations recorded by the microsensors in the three trials of phase 1.

An overview of the number of microsensors used in each trial can be seen in Table 3. The same microsensors A, T and D were used in trial 1 and 2. In trial 3, microsensors A and T had already been used in trial 1 and 2, while microsensors D had not been used in previous trials.

Table 3. Number of microsensors used in each Phase 1 trial

Sensor	Phase 1 – *in vitro*				
	Trial 1 (7 h in + 17 h out)/d for 30 d	**Trial 2** (2 h in + 1 h out + 2h in)/d for 30 d	**Trial 3** (embedded in material) (7 h in + 17 h out)/d for 30 d		
			Acrylic	**PVC**	**Thermoactive Acrylic**
A	30	30	3	3	3
T	20	20	3	3	3
D	16	16	3	3	3

3.1.1 Phase 1, Trial 1 results

In this trial, Sensor A (n = 30), Sensor T (n = 20) and Sensor D (n = 16) were placed in the water bath for 7 hours/day for 30 days. The scatter plots below (Figure 10, Figure 11and Figure 12) reveal the response difference of over- and under-estimations of the microsensors on each day of the trial, with twice the sensing interval threshold marked. The response difference scatter plot of Sensor A in trial 1 (Figure 10) showed that large number of deviations were recorded for multiple sensors on two days: 7 and 18. Since it is unlikely that all sensors malfunctioned on those two days, the deviations must be the results of assignable error that occurred during those days. Therefore, the data from all the sensors corresponding to those two days were not included in further data analysis. The other 12 data points that fell beyond twice the sensing interval were not excluded from the analysis. The data obtained from Sensor T in trial 1 show that 4 data points were recorded that were larger than twice the sensing interval (Figure 11). These points were not included in further data analysis. The data obtained from sensor D in trial 1 show that only 1 data point was recorded that was larger than twice the sensing interval (Figure 12). This point was not included in further data analysis.

Figure 10. Response difference scatter plots of Sensor A in Trial 1

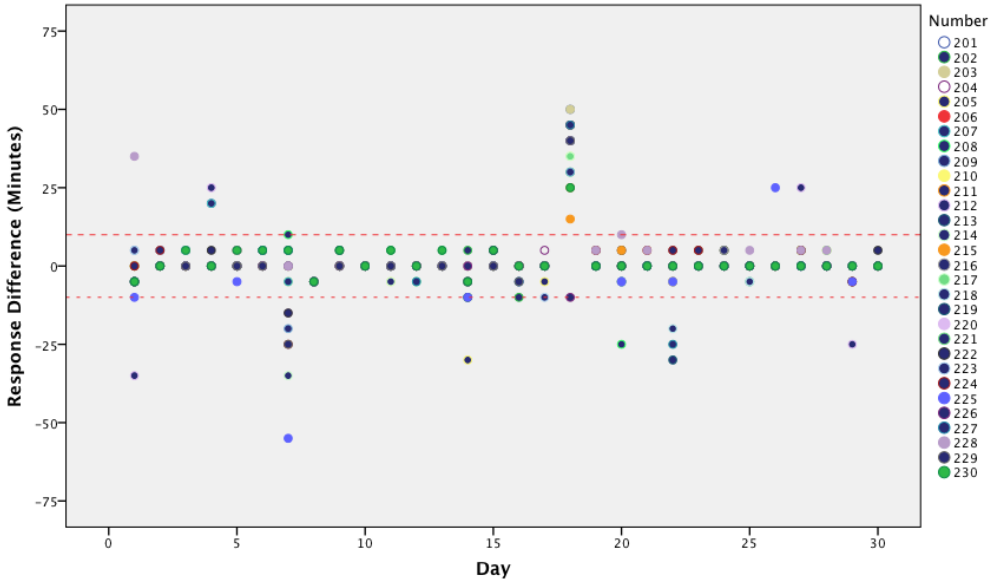


Figure 11. Response difference scatter plots of Sensor T in Trial 1

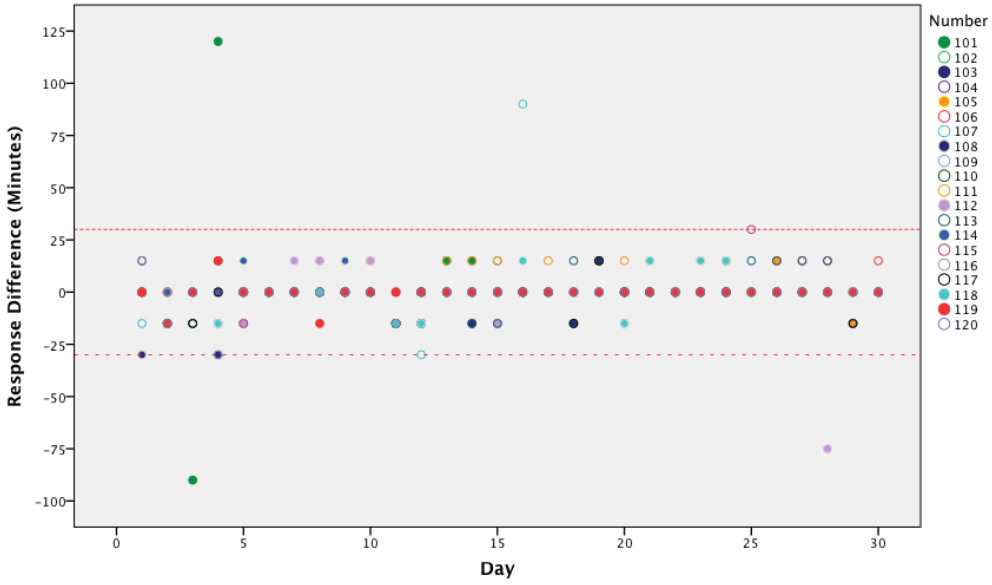
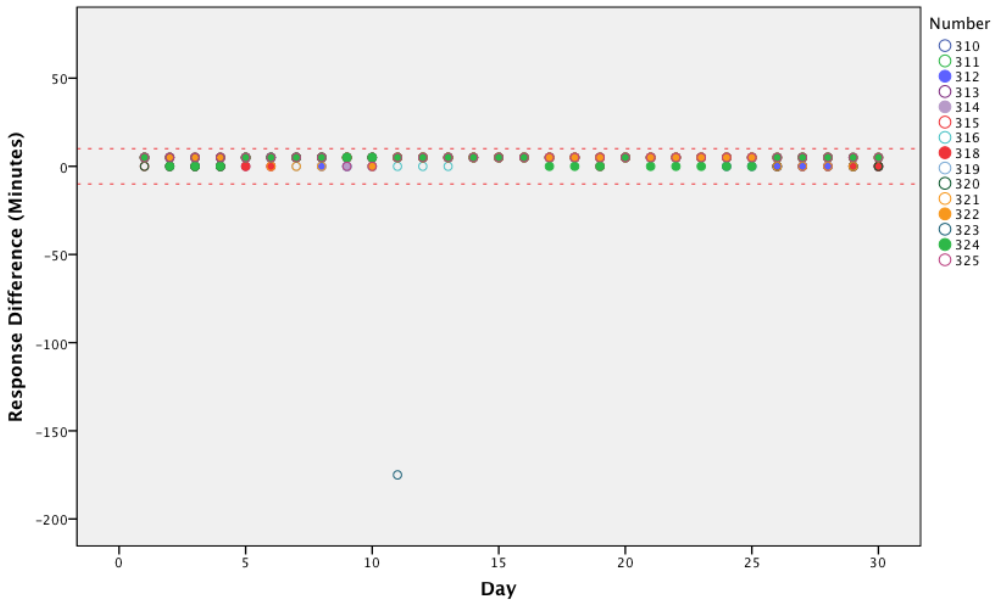


Figure 12. Response difference scatter plots of Sensor D in Trial 1



With the outliers removed, it was found that the mean absolute response difference for Sensor A in trial 1 was 1.67 ± 1.41 minutes, with a median absolute deviation of 0.00 minutes. Sensor T had a mean absolute response difference of 2.92 ± 6.31 minutes, with a median absolute deviation of 0.00 minutes. Sensor D had a mean response difference of 4.08 ± 4.64 minutes, with the largest median absolute deviation of 5.00 minutes. Descriptive results can be seen in Table 4. Scatter plots summarize the absolute response difference can be seen in Figure 13, Figure 14 and Figure 15.

Table 4. Descriptive results of the absolute response difference (minutes) for the microsensors in trial 1

Sensor	n	Mean (95% Confidence Interval)	Median absolute deviation	Maximum	Standard deviation (SD)	Standard error of mean (SEM)
A	840	1.67 (1.41, 1.94)	0.00	35.00	1.41	0.136
T	596	2.92 (2.41, 3.43)	0.00	30.00	6.31	0.26
D	430	4.08 (3.90, 4.27)	5.00	5.00	4.64	0.11

n= number of observations, with the outliers removed, recorded by the microsensors in the trial

Figure 13. Absolute response difference scatter plots of Sensor A in Trial 1

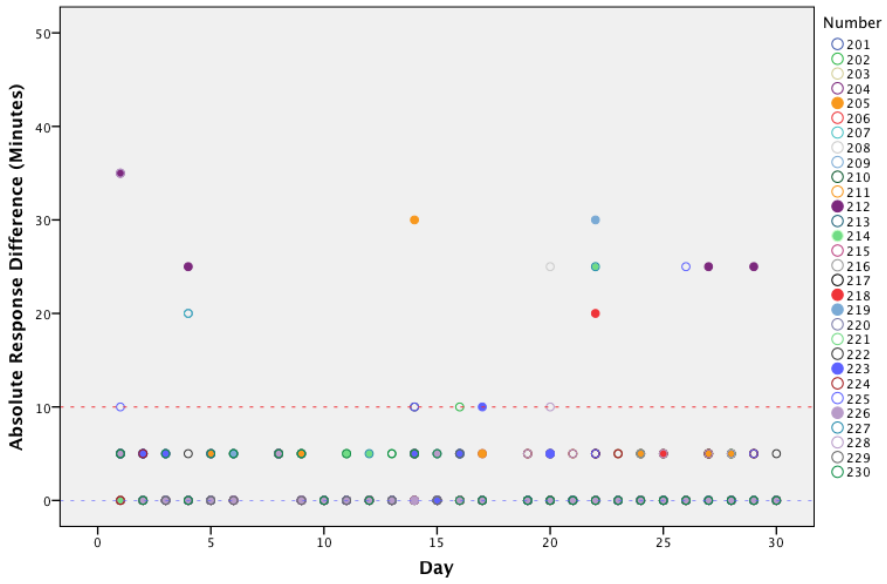


Figure 14. Absolute response difference scatter plots of Sensor T in Trial 1

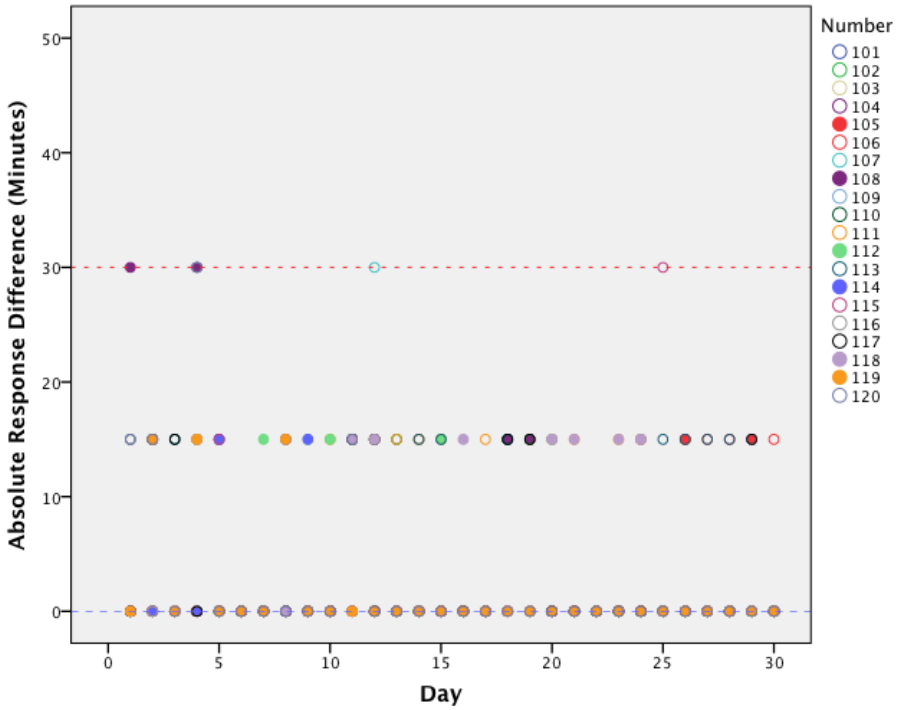
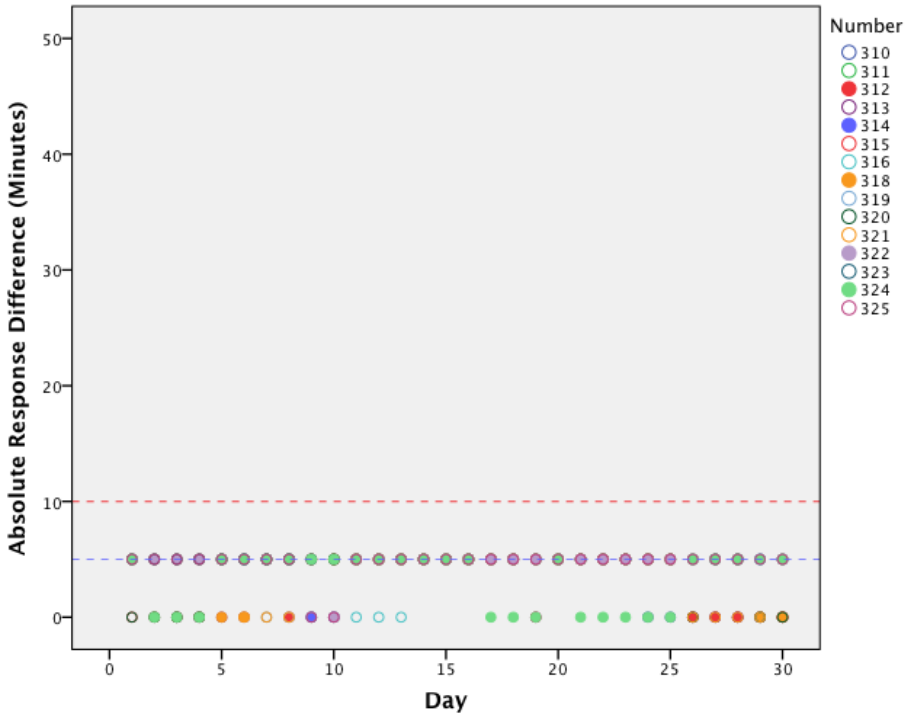
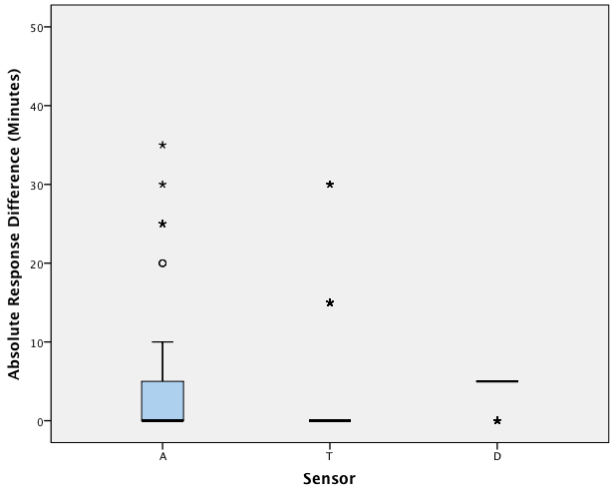


Figure 15. Absolute response difference scatter plots of Sensor D in Trial 1



A univariate ANOVA of the results showed a significant difference between the three sensors (F = 41.907, df = (2,1865), $p < 0.0001$). A Scheffé multiple mean comparison revealed that A < T < D. Figure 16 shows a boxplot of the absolute deviation results obtained in trial 1.

Figure 16. Boxplot of Phase 1, Trial 1



3.1.2 Phase 1, Trial 2 results

In trial 2, Sensor A (n = 30), Sensor T (n = 20) and Sensor D (n = 16) were inserted into the water bath for 2 hours, removed for 1 hour and reinserted into the water bath for 2 more hours for a total of 4hours/day "wear-time". The response difference scatter plots revealed that Sensor A in trial 2 had a deviation larger than twice the sensing interval recorded for a large number of sensors on three days: 1, 2 and 7 (Figure 17). Since it is unlikely that all sensors malfunctioned on those three days, the deviations must be the results of assignable error that occurred during those days. Therefore, the data from all the sensors corresponding to those three days were not included in further data analysis. The other 3 data points that fell beyond twice the sensing interval were not excluded from the analysis. The data obtained from Sensor T in trial 2

show that only 2 data points were recorded that were larger than twice the sensing interval. These points were not included in further data analysis (Figure 18). The data obtained from Sensor D in trial 2 show that a very large number of data points were recorded that were larger than twice the sensing interval on multiple days; no exclusions were made and all data were included in analysis (Figure 19).

Figure 17. Response difference scatter plot of Sensor A in Trial 2

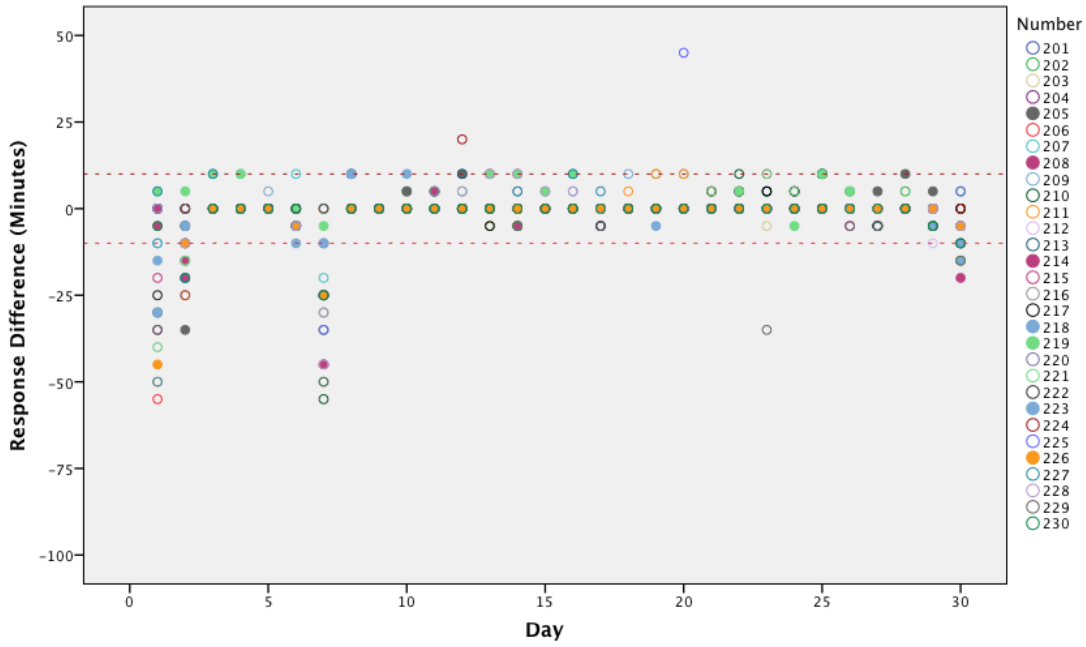


Figure 18. Response difference scatter plot of Sensor T in Trial 2

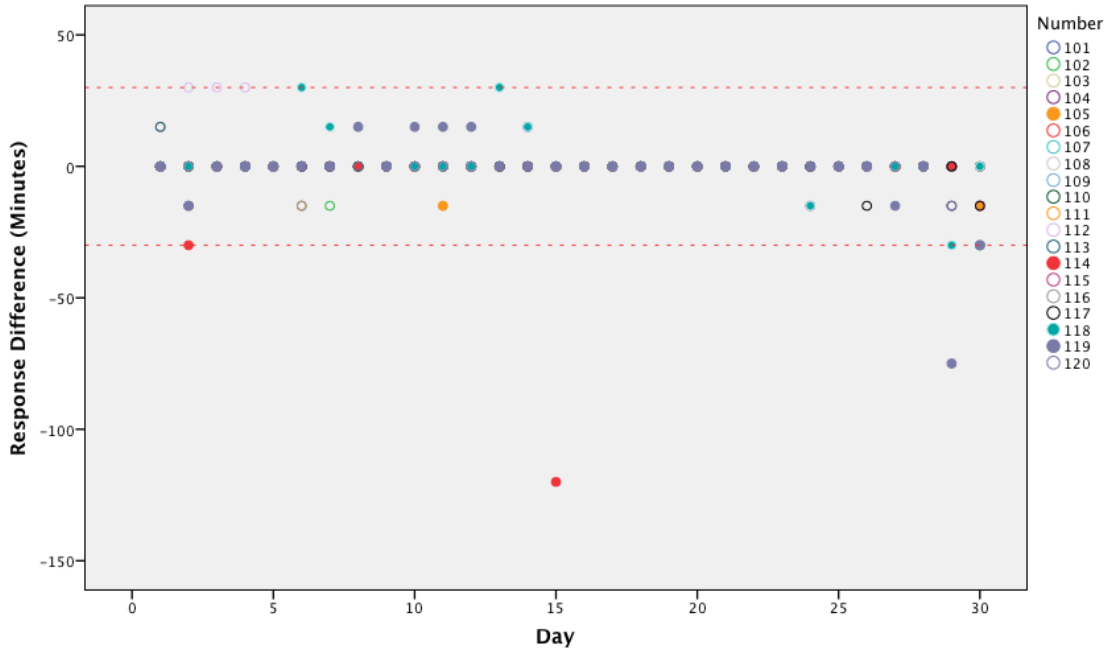
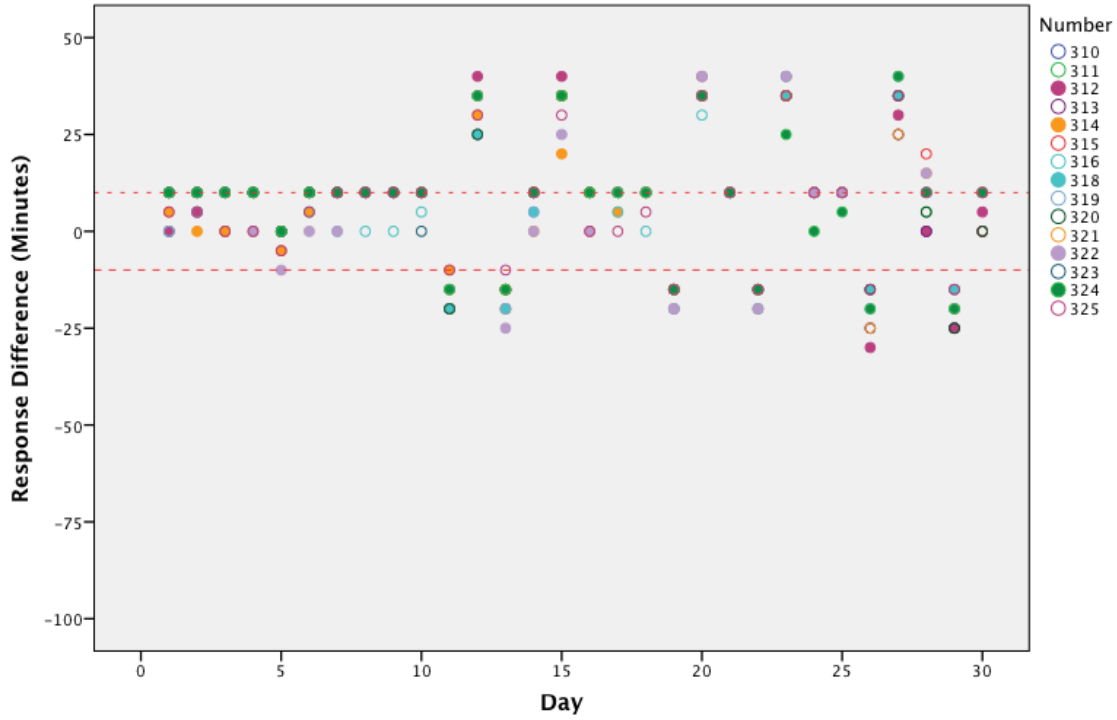


Figure 19. Response difference scatter plot of Sensor D in Trial 2



With the outliers removed, it was found that the mean absolute response difference for Sensor A in trial 2 was 1.41 ± 3.60 minutes, with a median absolute deviation of 0.00 minutes. Sensor T had a mean absolute response difference of 1.35 ± 5.10 minutes, with a median absolute deviation of 0.00 minutes. Sensor D had a mean response difference of 14.07 ± 10.20 minutes, with the largest median absolute deviation of 10.00 minutes. Descriptive results are presented in Table 5. Scatter plots summarize the absolute response difference can been seen in Figure 20, Figure 21 and Figure 22.

Table 5. Descriptive results of the absolute response difference (minutes) for the microsensors in trial 2

Sensor	n	Mean (95% Confidence Interval)	Median Absolute Deviation	Maximum	Standard deviation (SD)	Standard error of mean (SEM)
A	810	1.41 (1.17, 1.66)	0.00	45.00	3.60	0.13
T	598	1.35 (0.94, 1.76)	0.00	30.00	5.10	0.21
D	430	14.07 (13.10, 15.04)	10.00	40.00	10.20	0.49

n= number of observations, with the outliers removed, recorded by the microsensors in the trial

Figure 20. Absolute response difference scatter plot of Sensor A in Trial 2

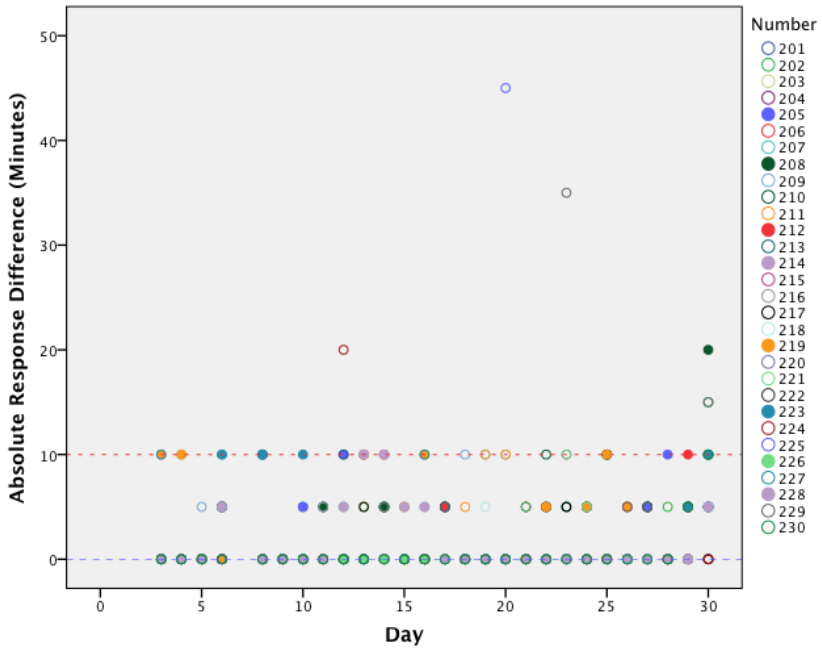


Figure 21. Absolute response difference scatter plot of Sensor T in Trial 2

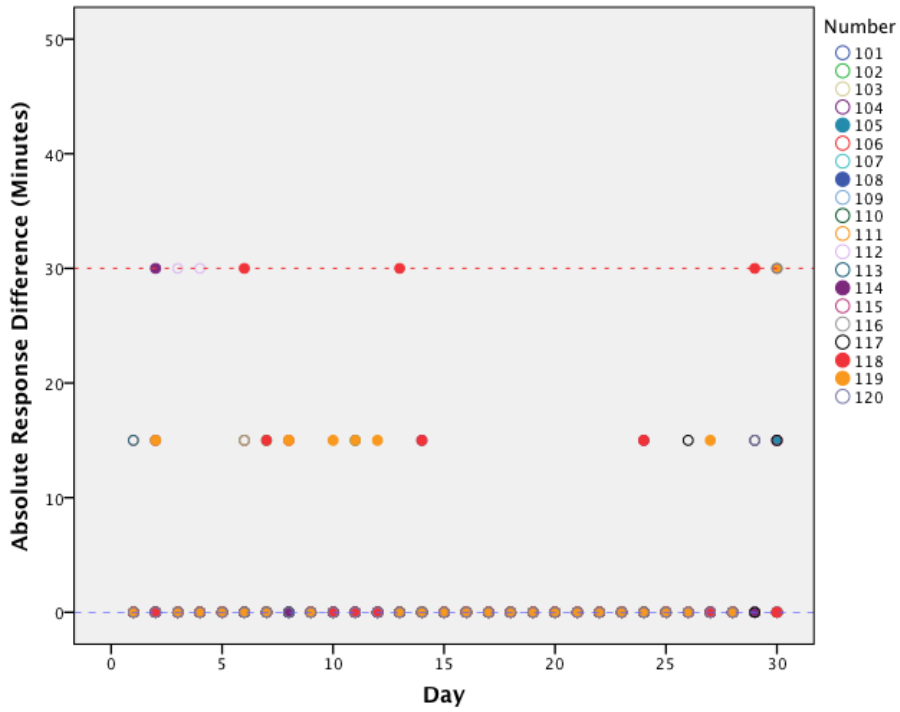
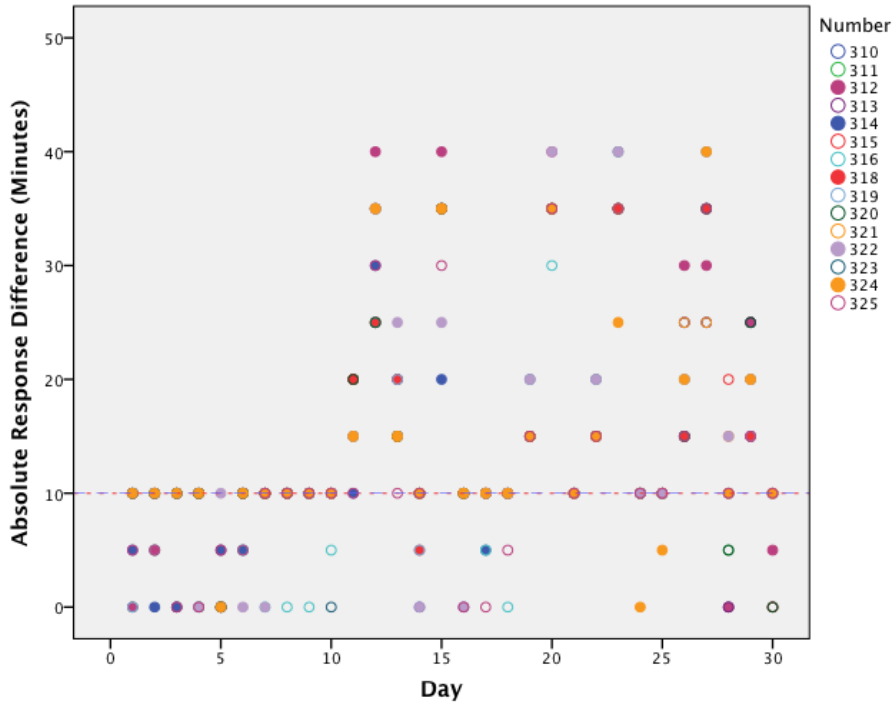
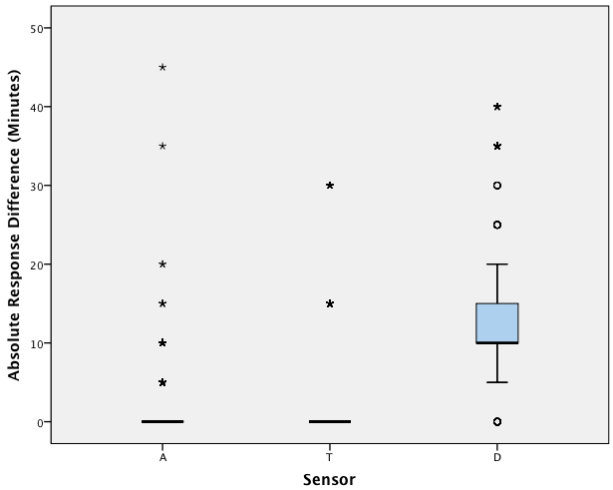


Figure 22. Absolute response difference scatter plot of Sensor D in Trial 2



A univariate ANOVA of the results showed a significant difference between the three sensors ($F = 688.07$, $df = (2, 1837)$, $p < 0.0001$). A Scheffé multiple mean comparison revealed that A = T < D. Figure 23 shows a boxplot of the absolute deviation results obtained in trial 2.

Figure 23. Boxplot of Phase 1, Trial 2



3.1.3 Phase 1, Trial 3 results

In trial 3, the effect of different embedding materials on sensor readings was tested. Sensor A (n = 9), Sensor T (n = 9) and Sensor D (n = 9) were embedded into 3 materials: acrylic (n = 3/Sensor), PVC (n = 3/Sensor) and thermoactive acrylic (n = 3/Sensor). The blocks were placed in the water bath for 7 hours/day for 30 days. All data obtained from Sensor A in trial 3 fell within twice the sensing interval; no outliers were removed (Figure 24). The data from Sensor T in trial 3 showed that only 1 data point recorded was larger than twice the sensing interval. This point was not included in further data analysis (Figure 25). All data obtained from Sensor D in trial 3 fell within twice the sensing interval; no outliers were removed (Figure 26). However, as previously mentioned, Sensor D 301, which was embedded in acrylic material, battery died prematurely and only 15 of the 30 days were recorded.

Figure 24. Deviation scatter plot of Sensor A in Trial 3

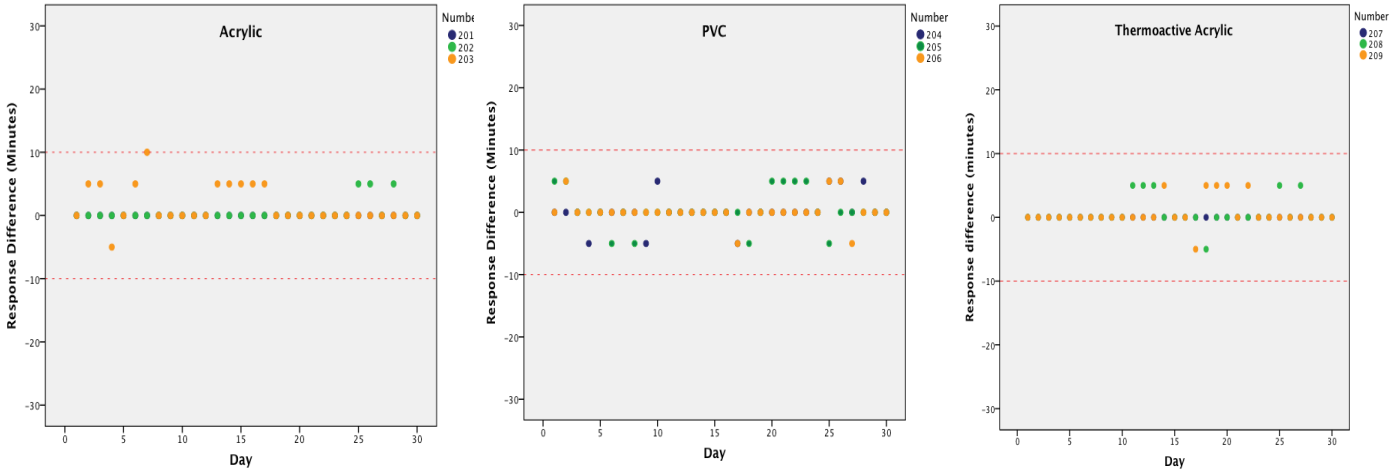


Figure 25. Deviation scatter plot of Sensor T in Trial 3

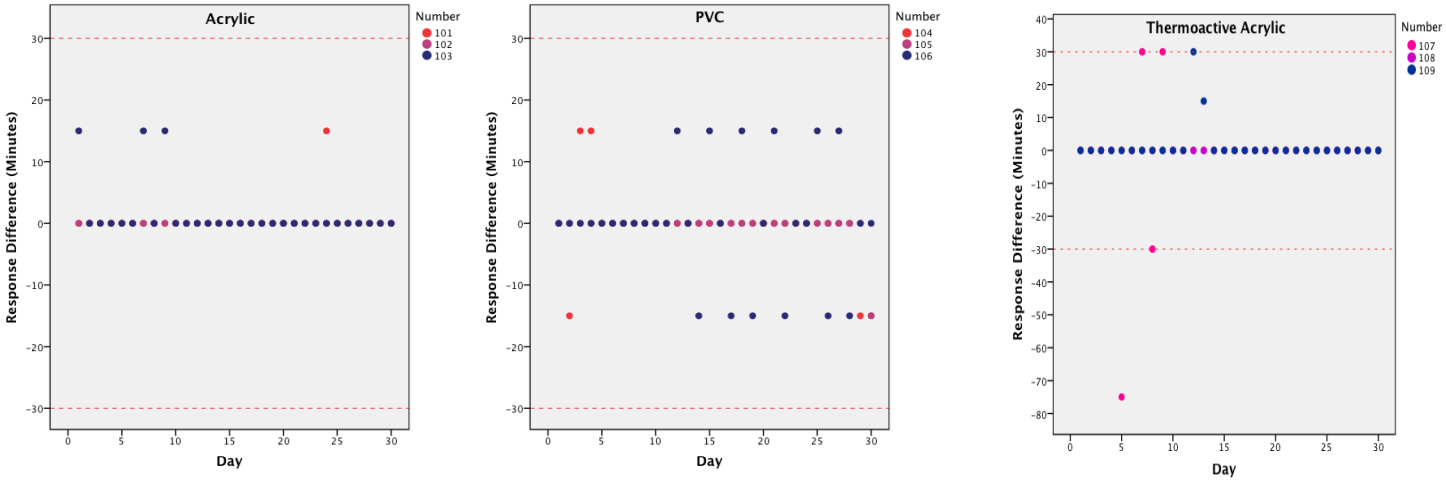
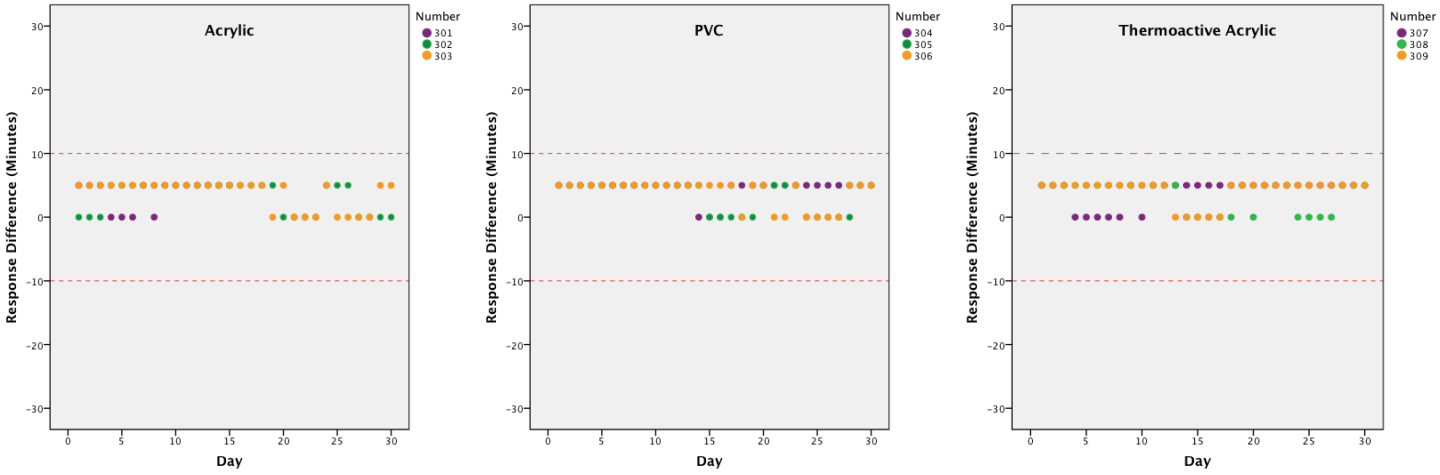


Figure 26. Deviation scatter plot of Sensor D in Trial 3



The absolute response difference for Sensor A was 0.78 ± 1.20 minutes, 1.22 ± 2.16 minutes, and 0.67 ± 1.71 minutes when embedded into acrylic, PVC and thermoactive acrylic, respectively. The median absolute deviations in all three materials were 0.00 minutes. Sensor T

had a mean absolute response deviation of 0.67 ± 3.11 minutes, 3.00 ± 6.04 minutes and 1.52 ± 6.41 minutes when embedded into acrylic, PVC and thermoactive acrylic, respectively. The median absolute deviations in all three materials were 0.00 minutes. Sensor D had a mean response difference of 3.47 ± 2.32 minutes, 3.89 ± 2.09 minutes and 3.83 ± 2.13 minutes when embedded into acrylic, PVC and thermoactive acrylic, respectively. The median absolute deviations in all three materials were 5.00 minutes. Descriptive results are presented in Table 6. Scatter plots summarize the absolute response difference can be seen in Figure 27, Figure 28 and Figure 29.

Table 6. Descriptive results of the absolute response difference (minutes) for the microsensors embedded in different materials in trial 3

Sensor	Material	n	Mean (95% Confidence Interval)	Median absolute deviation	Maxi-mum	Standard deviation (SD)	Standard error of mean (SEM)
A	Acrylic	90	0.78 (0.37, 1.19)	0.00	10.00	1.20	0.21
	PVC	90	1.22 (0.77, 1.67)	0.00	5.00	2.16	0.23
	Thermoactive acrylic	90	0.67 (0.31, 1.02)	0.00	5.00	1.71	0.18
T	Acrylic	90	0.67 (0.02, 1.32)	0.00	15.00	3.11	0.33
	PVC	90	3.00 (1.74, 4.26)	0.00	15.00	6.03	0.64
	Thermoactive acrylic	89	1.52 (0.17, 2.87)	0.00	30.00	6.41	0.68
D	Acrylic	75	3.47 (2.93, 4.00)	5.00	5.00	2.32	0.27
	PVC	90	3.89 (3.45, 4.33)	5.00	5.00	2.09	0.22
	Thermoactive acrylic	90	3.83 (3.39, 4.28)	5.00	5.00	2.13	0.22

n= number of observations, with the outliers removed, recorded by the microsensors in the trial

Figure 27. Absolute response difference scatter plots of Sensor A in Trial 3

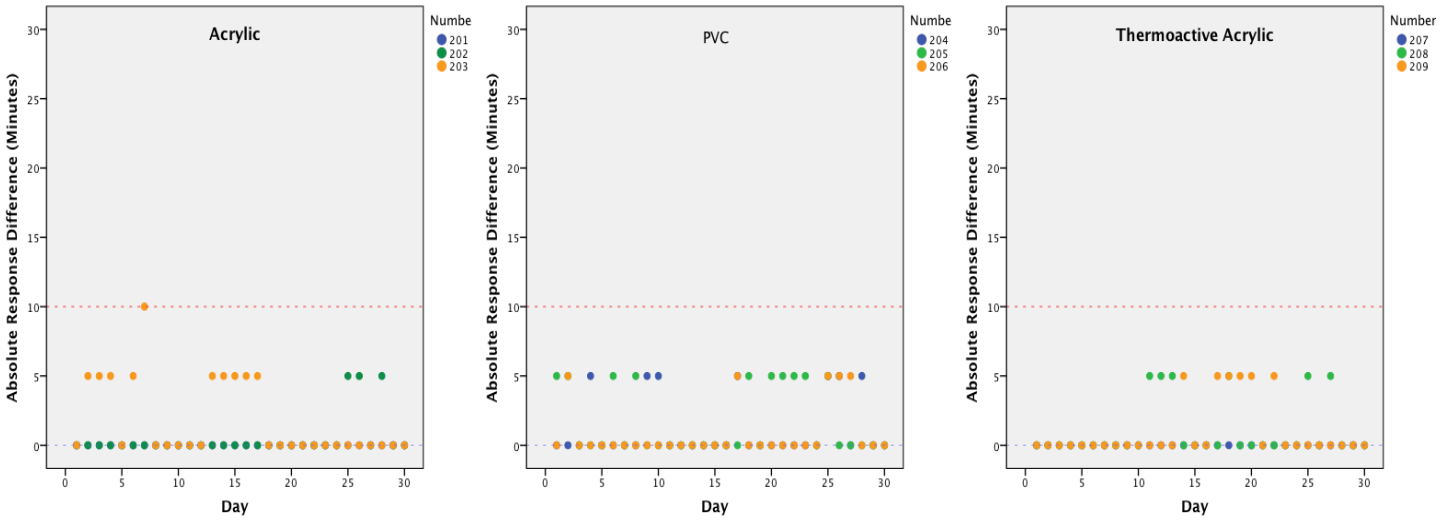


Figure 28. Absolute response difference scatter plots of Sensor T in Trial 3

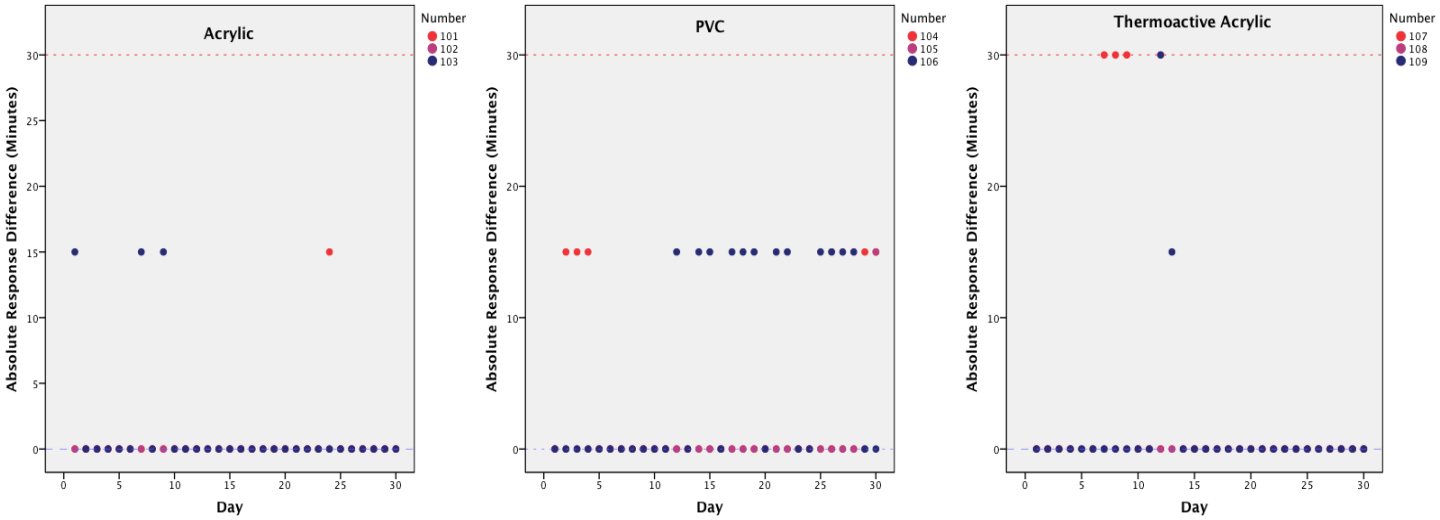
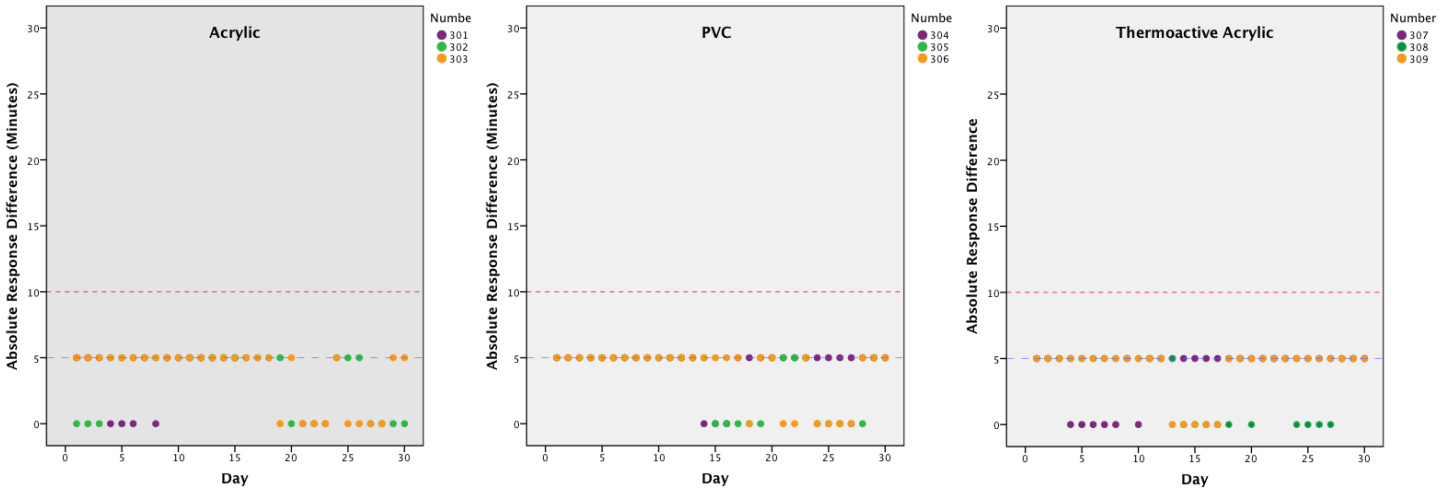
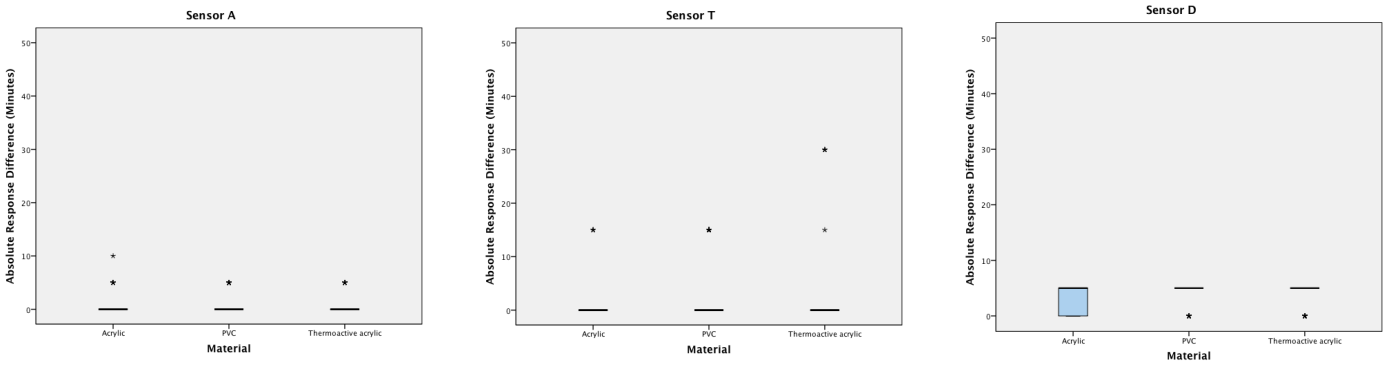


Figure 29. Absolute response difference scatter plots of Sensor D in Trial 3



A univariate ANOVA of the results showed no significant difference in Sensor A's recording due to the three embedding materials (F = 2.03, df (2, 269), $p = 0.133$). Sensor T results showed a significant difference due to the three embedding materials (F = 4.32, df (2, 268), $p < 0.05$). A Scheffé multiple mean comparison revealed that acrylic = thermoactive acrylic < PVC = thermoactive acrylic. There was no significant difference due to the three embedding materials for Sensor D (F = 0.88, df (2, 254), $p = 0.41$). Boxplots of the absolute response differences for Sensor A, T and D for Trial 3 are presented in Figure 30.

Figure 30. Boxplots of absolute response difference of the sensors in Trial 3



3.1.5 Quality control

To assess for quality control, the microsensors were kept out of the water bath for 30 days and it was assessed if they recorded any "wear-time". Several microsensors had a few readings above the temperature cutoff. They are shown in Appendix D. Out of 2250 observations, only 27 observations during this trial period found the microsensors recording "wear-time" while they were not in the water bath or mouth. These false positive readings occurred most frequently for Sensor D 317, which was previously reported to have erroneous readings and was removed from the analysis. Twenty-five percent of Sensor A microsensors recorded at least one erroneous observation of increased temperature during the control period. This represented 0.09% of the total number of observations Sensor A microsensors recorded during this period. 23.4% of Sensor T microsensors record at least one observation of increased temperature during the control period. This was 1% of all the observations Sensor T microsensors made during this trial. Sensor D had the most microsensors recording erroneous temperatures at 28% of the microsensors. This represented 1.8% of the total number of observations Sensor D microsensors made during this control trial. The proportion of microsensor units and the number of observations per sensor types that recorded false positives is summarized in Table 7).

Table 7. Number of microsensor units and observations that reported false positive during control trial

	Sensor A	Sensor T	Sensor D
Number of microsensors involved in error	5/20	7/30	7/25
	25%	23.4%	28%
Number of observations involved in error	5/600	9/900	13/750
	0.9%	1%	1.8%

The calculation of specificity was used to determine the probability that a test result will be negative when the condition is not present (i.e. out of the hot water bath). It was found that the three microsensors were highly specific with values of 99.17%, 99.01% and 98.3% for Sensor A, T and D, respectively (Table 8).

Table 8. Specificity and confidence interval for the three microsensors

Sensor type	Specificity	95% confidence interval
A	99.01	98.13-99.55
T	99.17	98.08-99.73
D	98.3	97.10-99.09

Index of agreement (R)[14, 102] between the microsensor recordings and the logged time was calculated for each microsensor type in phase 1. It was found that all three microsensors had a strong reliability in their recording capabilities. The index of agreement for Sensor A, T and D was 0.995, 0.996 and 0.976 respectively. This is summarized below in Table 9.

Table 9. Index of agreement

Sensor	Index of Agreement (R)
A	0.995
T	0.996
D	0.976

3.2 Phase 2: *In vivo* testing

Fourteen volunteers from The University of British Columbia Dental School participated in the study. There were eight males and six females and the mean age of the participants was 27.9 ± 2.78 years (range 24.5 years to 35.5 years). (Summarized demographics data can be found

in Table 10.) There were five subjects who described themselves as daytime or nighttime mouth breathers, four reported having dry mouth in the mornings, six reported snoring and grinding their teeth at night, one subject has asthma, five have seasonal allergies and only one reported having OSA and used a CPAP nightly. Nine subjects reported having worn appliances in the past, such as a nigh guard or an orthodontic retainer.

Table 10. Summary of demographics of the total 14 subjects

	n
Males	8
Females	6
Mean age (years)	27.9 ± 2.78
Age range (years)	24.5 – 35.5
Mouth breathers	5
Dry Mouth	4
Snorers	6
Bruxism	6
Asthma	1
Seasonal allergies	5
Obstructive sleep apnea	1
Past history of appliance wear	9

The number of nights the vacuum formed retainer with the embedded microsensors was worn varied between subjects. This is because the Sensor A divides each day from midnight to midnight and Sensor D divides each day from noon to noon. Therefore, if a subject wore the appliance from 10:00 PM to 7:00 AM, Sensor A would record two hours on the day before and seven hours for the next day. Sensor D, on the other hand, would consider the same interval as one night's wear for a total of nine hours. Thus, the amount of nights the appliance was worn appears to differ for each microsensor type within one subject because of the different cutoff

times. The number of hours reported from the subjects' logs was calculated per day or per night, depending on the sensor type. Two participants terminated the trial prematurely. One subject only completed 23 nights as she graduated and moved out of town prior to completion of the trial. Another subjected only completed 16 nights as she had difficulty wearing the appliance at night due to discomfort. The remaining 12 subjects completed the full trial. The number of days each subject wore the appliance varied from 16 to 36 and is summarized in Table 11.

Table 11. Number of days subjects wore appliance according to Sensor A and Sensor D

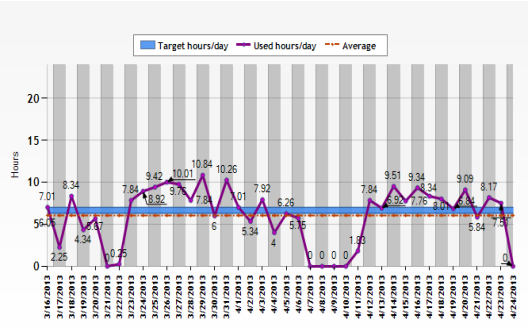
Subject	Days according to Sensor A	Days according to Sensor D
S301	33	30
S302	30	30
S303	30	30
S304	34	30
S305	31	30
S306	27	23
S307	32	30
S308	30	30
S309	30	30
S310	30	30
S311	31	31
S312	32	30
S313	17	16
S314	36	30

All 28 microsensors used recorded accurate pre-test and post-test times. As such, data from all subjects' microsensors were included in the analysis. Data was taken from the graphs that the software of Sensor A and Sensor D produced. An example of what the graphs from the software look like can be seen below in Figure 31. Scatter plots of the response differences are seen in Figure 32 and Figure 33. Deviations larger than 60 minutes (green lines on scatter plot),

17 observations from Sensor A and 16 observations from Sensor D, were removed and not included in further analysis.

Figure 31. Example of computed graphs from the microsensors

A. Sensor A graph



B. Sensor D graph

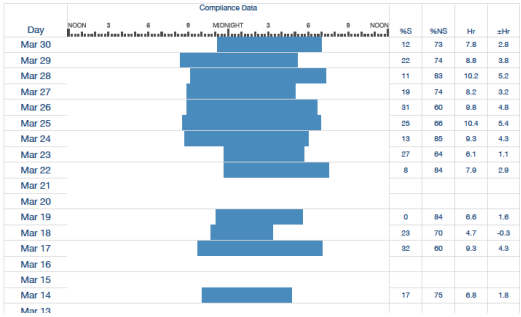


Figure 32. Response difference scatter plot of Phase 2 data for Sensor A

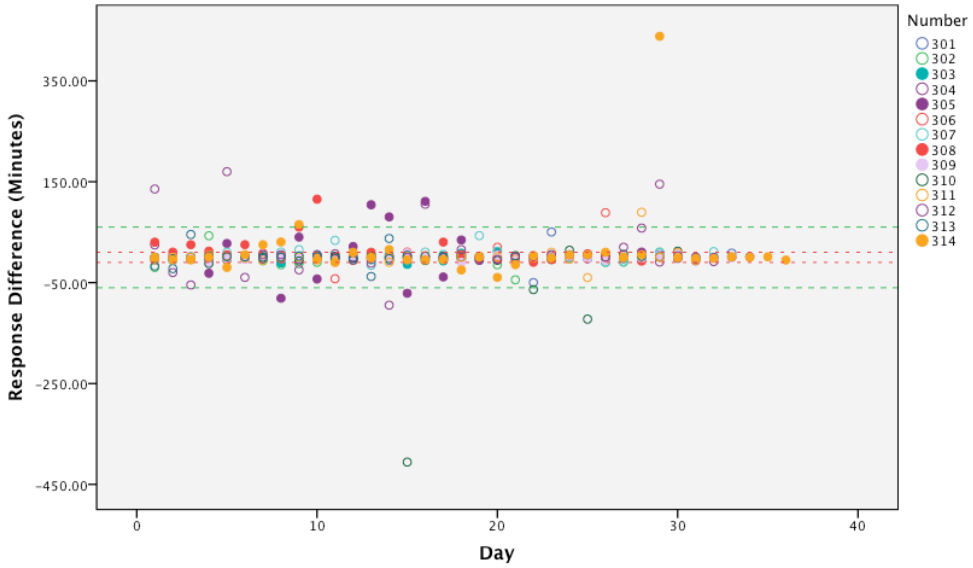
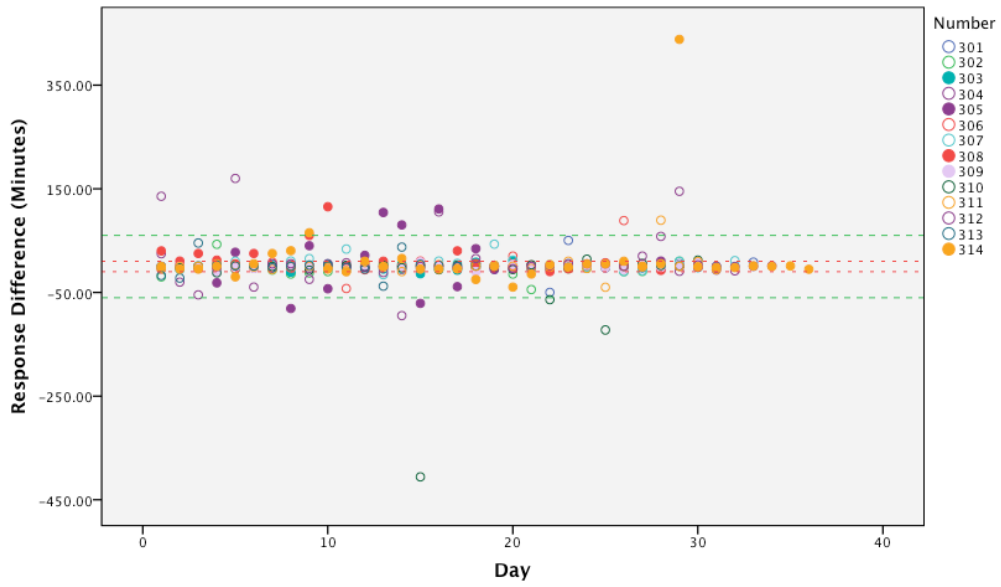


Figure 33. Response difference scatter plot of Phase 2 data for Sensor D



The mean absolute response difference for Sensor A in Phase 2 was 6.32 ± 10.08 minutes, with median absolute deviation of 3.00 minutes. The mean absolute difference for Sensor D was 6.81 ± 8.05 minutes, with a median absolute deviation of 5.00 minutes. The descriptive statistics of the two microsensors used in the *in vivo* phase are presented in Table 12. Figure 34 and Figure 35 are scatter plots of the absolute response difference of Sensor A and D in phase 2.

Table 12. Descriptive statistics of the absolute response difference (minutes) in Phase 2

Sensor	n	Mean (95% Confidence interval)	Median absolute deviation	Maximum	Standard deviation (SD)	Standard error of mean (SEM)
A	376	6.32 (5.30, 7.34)	3.00	58.20	10.08	1.83
D	360	6.81 (5.98, 7.65)	5.00	56.00	8.05	0.42

n= number of observations, with the outliers removed, recorded by the microsensors in the trial

Figure 34. Absolute response difference scatter plot of Sensor A in Phase 2

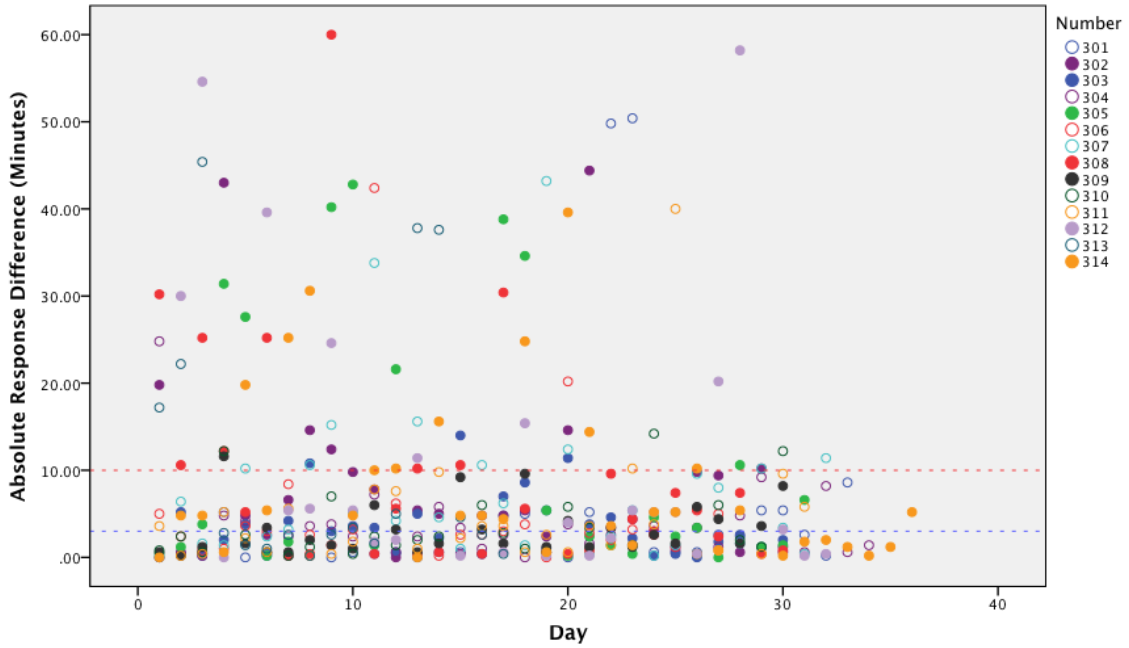
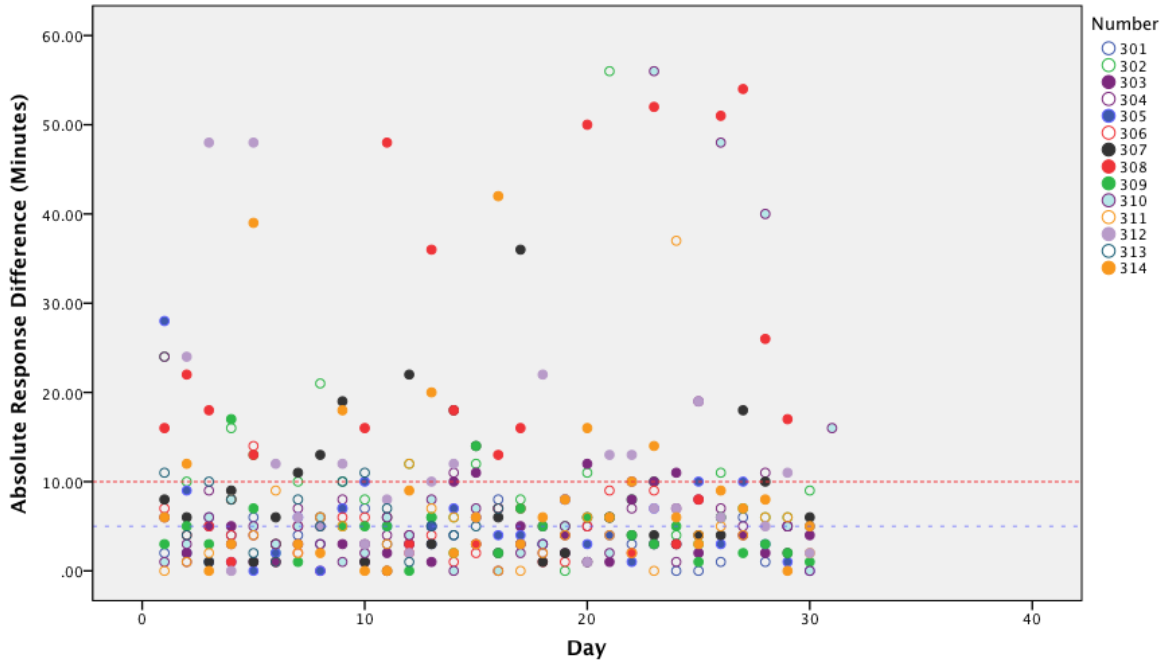


Figure 35. Absolute response difference of Sensor D in Phase 2



A univariate ANOVA found that there was a statistical difference between the microsensor types in Phase 2 ($F = 6.41$, df (13, 383), $p < 0.001$). A post hoc Scheffé multiple mean comparison revealed that subject 308 was significantly different than the other subjects (further detail on this is reported in 3.3 Case report). The analysis was repeated removing subject 308 and it was found that there was no statistical difference between Sensor A and D in Phase 2 ($F = 0.54$, df (1, 735), $p = 0.45$). Absolute response difference scatter plots for the two sensors types and a box plot of all the data with subject 308 removed are presented in Figure 36, Figure 37 and Figure 38, respectively.

Figure 36. Absolute response difference scatter plot for Sensor A in Phase 2 with Subject 308 removed

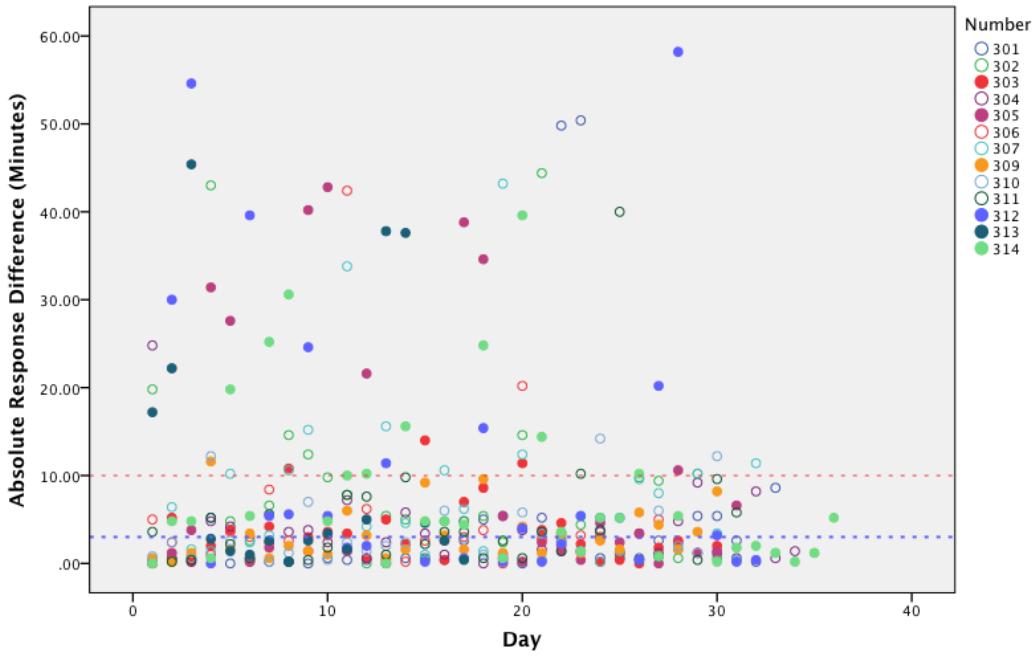


Figure 37. Absolute response difference scatter plot for Sensor D in Phase 2 with Subject 308 removed

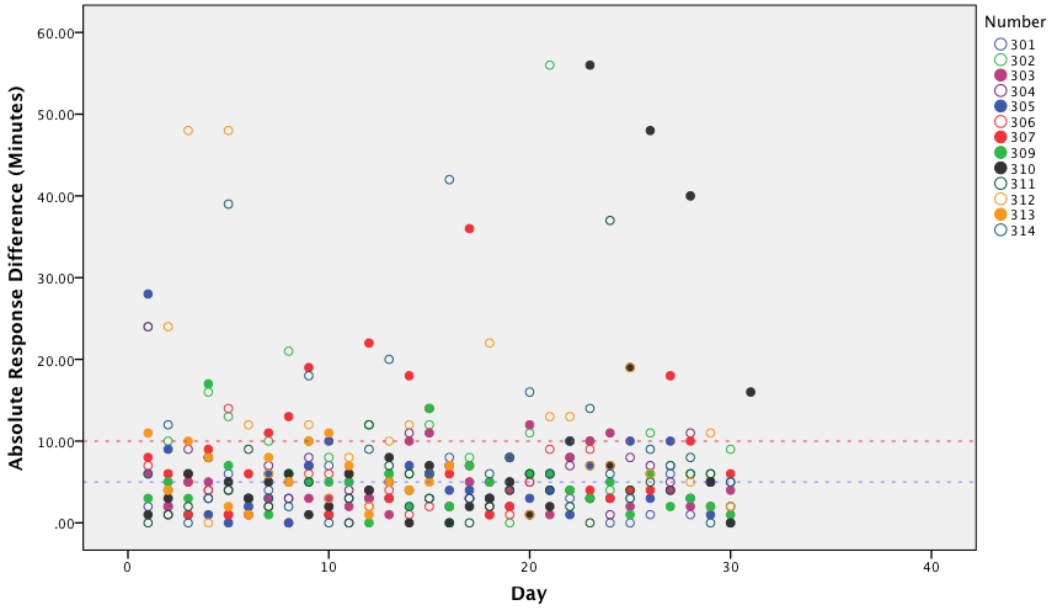
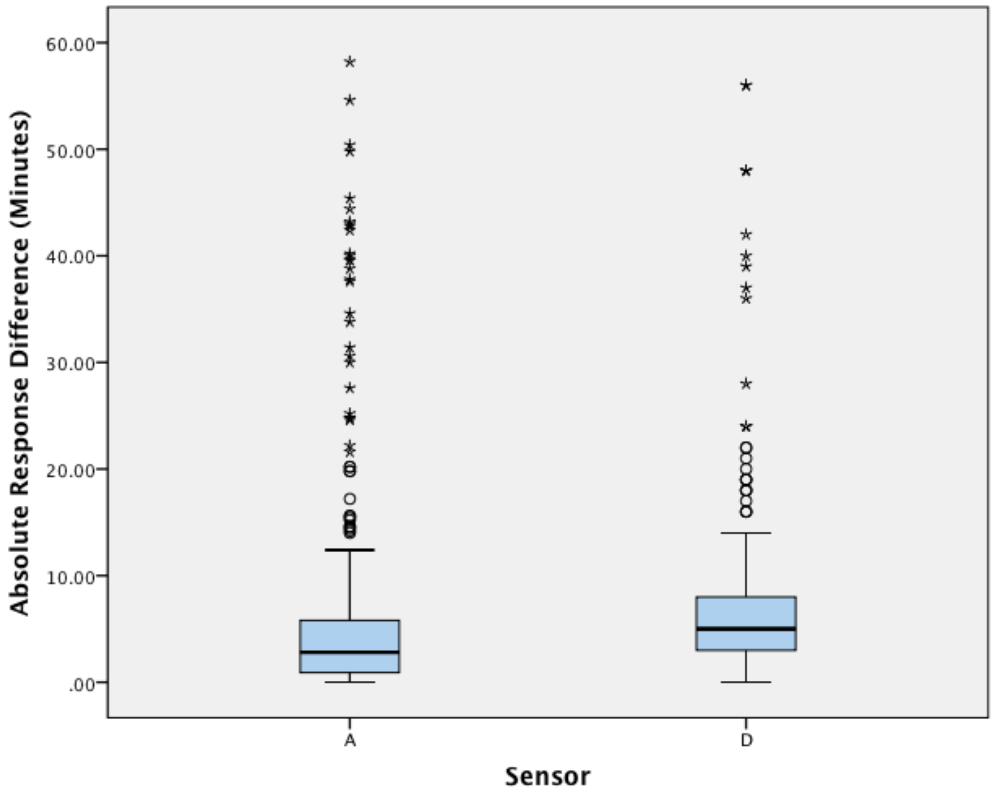


Figure 38. Box plot of absolute response difference of Sensor A and D in Phase 2



3.3 Combined trials

An analysis of the response difference data for each of the sensors in the 19 experimental groups was performed to identify the frequency of negative, zero and positive deviations. This represents the amount of underestimation, no difference and overestimation of "wear-time" that the microsensors recorded. No deviation was defined as response difference of 0.00 minutes. Sensor A recorded no deviation for 74.40% to 82.90% of the time in phase 1 *in vitro* testing. Sensor T had no deviation for 81.54% to 95.65% of time in phase 1. Sensor D had no deviation for 10.23% to 25.10% of the time and overestimated "wear" the majority of the time, from 69.30% to 81.63%, in phase 1.

In Phase 2, the two sensors performed equally well, with Sensor A having responses falling within two sensing intervals (-10 to +10 minutes) 82.72% of the time and Sensor D 81.77% of the time. However, the median of the absolute deviations for Sensor A was smaller than that of Sensor D (3.00 minutes versus 5.00 minutes, respectively). To put the results into perspective, the cumulative log time in Phase 2 was 156313 minutes (~2605 hours or ~108 days); Sensor A showed a cumulative absolute deviation of 2652 minutes (~44 hours or ~1.8 days), which translates into an overall error of less than 2%. Sensor D showed a cumulative absolute deviation of 2948 minutes (~49 hours or ~2 days), which also translates into an overall error of less than 2%. The results are summarized in Table 13. Table 14 summarizes the number of cases in which each sensor had readings outside twice the sensing interval range.

Table 13. Deviation frequency analysis (in %)

Sensor	Phase 1 – *in vitro*									Phase 2 – *in vivo* 30 d		
	Trial 1 (7 h in + 17 h out)/d for 30 d			Trial 2 (2 h in + 1 h out + 2h in)/d for 30 d			Trial 3 (material) (7 h in + 17 h out)/d for 30 d					
Deviation	**-**	**0**	**+**	**-**	**0**	**+**	**-**	**0**	**+**	**<-10**	**-10 to +10**	**>+10**
A	13.21	74.40	12.38	9.51	80.86	9.63	4.46	82.90	12.64	6.91	82.72	10.37
T	10.57	81.54	7.89	4.68	92.64	2.68	4.35	95.65	5.95	-	-	-
D	0.00	18.37	81.63	20.47	10.23	69.30	0.00	25.10	74.90	8.07	81.77	10.16

Table 14. Number of deviations outside twice the sensing interval recorded

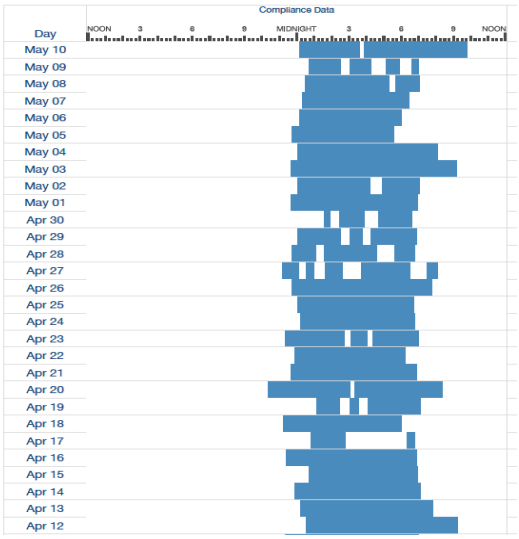
Sensor	Phase 1 – *in vitro*			Phase 2- *in vivo*
	Trial 1 (7 h in + 17 h out)/d for 30 d	**Trial 2** (2 h in + 1 h out + 2h in)/d for 30 d	**Trial 3** (embedded) (7 h in + 17 h out)/d for 30 d	
A	14	8	0	70
T	0	0	0	-
D	0	154	0	70

3.3 Case report

One of the participants during Phase 2 was a 25-year-old male diagnosed with mild OSA, who was wearing a CPAP every night to sleep. For 30 nights, the subject wore the maxillary vacuum formed retainer appliance with Sensor A and Senor D embedded on the buccal shelves concurrently with his CPAP. Further investigation was done into this patient because of the interesting appearance of his adherence graph computed by Sensor D, which can be seen in (Figure 39). It appeared from the graph of the Sensor D that the subject was wearing the appliance (blue bars) and removing the appliance (white) throughout the night. However, the log

revealed that the appliance was worn continuously. Through questioning the subject, it was determined that the subject was in fact wearing the appliance throughout the night and denied removing it periodically after insertion.

Figure 39. Adherence graphs for Sensor D for patient wearing OA combined with CPAP



Examination of the raw data revealed that the temperature in the subject's mouth dropped below 33.5^0C which is the cutoff point for Sensor D's algorithm of wear. The temperature drop occurred periodically throughout the subject's sleep and correlates to the non-wearing time (white area) seen on the graph. Figure 40, below depicts the inconsistent temperature and the spikes and dips seen in oral temperature of this subject on day 12 of the trial (used as an example), which corresponds to the wear-time calculated, as seen in Figure 41. This differs greatly from the typical temperature variations found in the mouth over a period of time (Figure 42), which is much more consistent with no sharp spikes and drops in temperature.

Figure 40. Temperature variation recorded by Sensor D on Day 12 of the trial

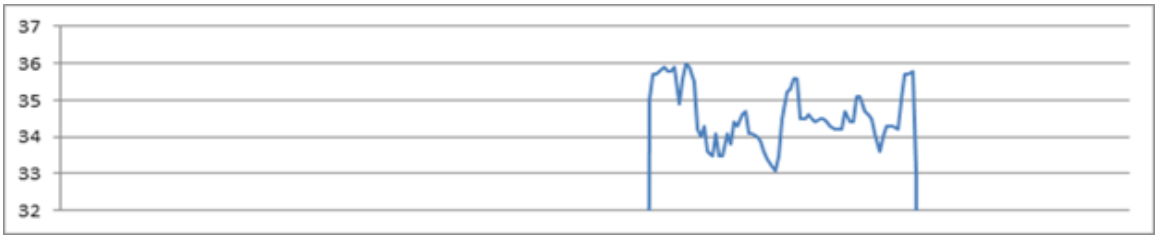
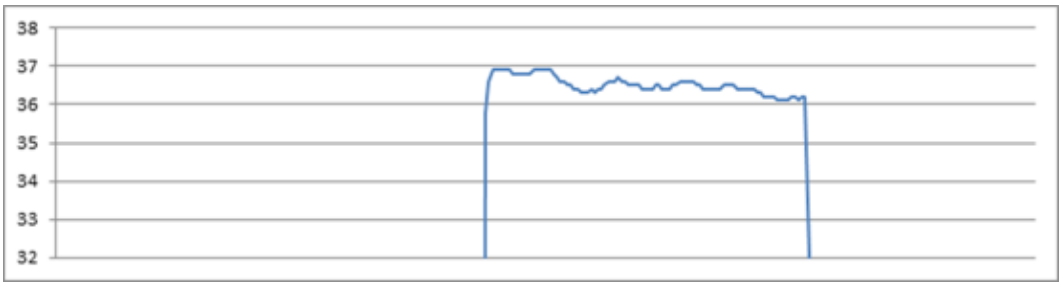


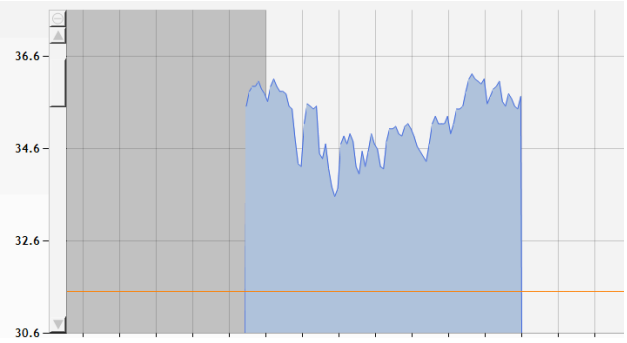
Figure 41. Corresponding wearing data of Sensor D on Day 12 (0 = no wear, 1 = wear)

Figure 42. Typical temperature variation seen in the mouth



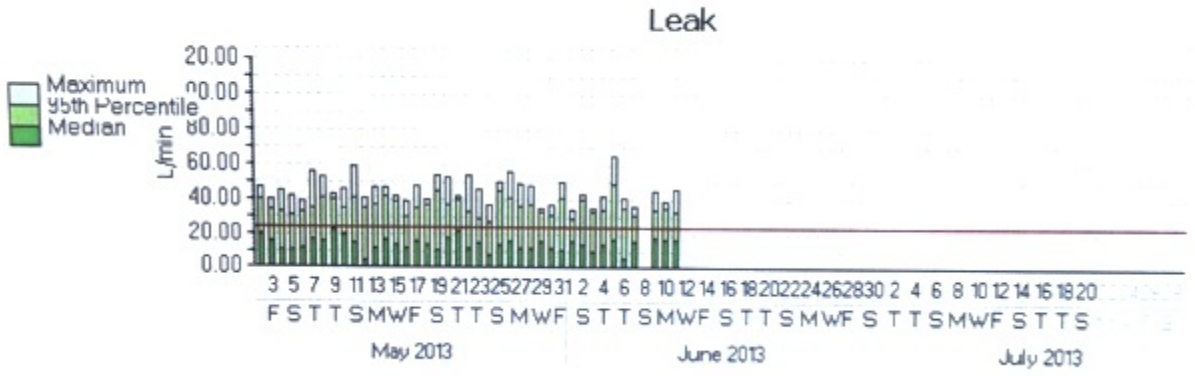
The adherence graph for Sensor A matched more closely to the log provided by the subject. In Figure 43, the temperature variation for Day 12 of the trial recorded by Sensor A is shown. The graph is very similar to the temperature variation recorded by Sensor D (Figure 40). However, the red line depicting the temperature threshold is at 31.5^0. This means that all temperatures above this are including in the wear calculation. A threshold of 33.5^0C, as in Sensor D, would mean that at certain time points the temperature drops below this, which corresponds to the appliance not being worn.

Figure 43. Temperature variation recorded by Sensor A on Day 12 of the trial



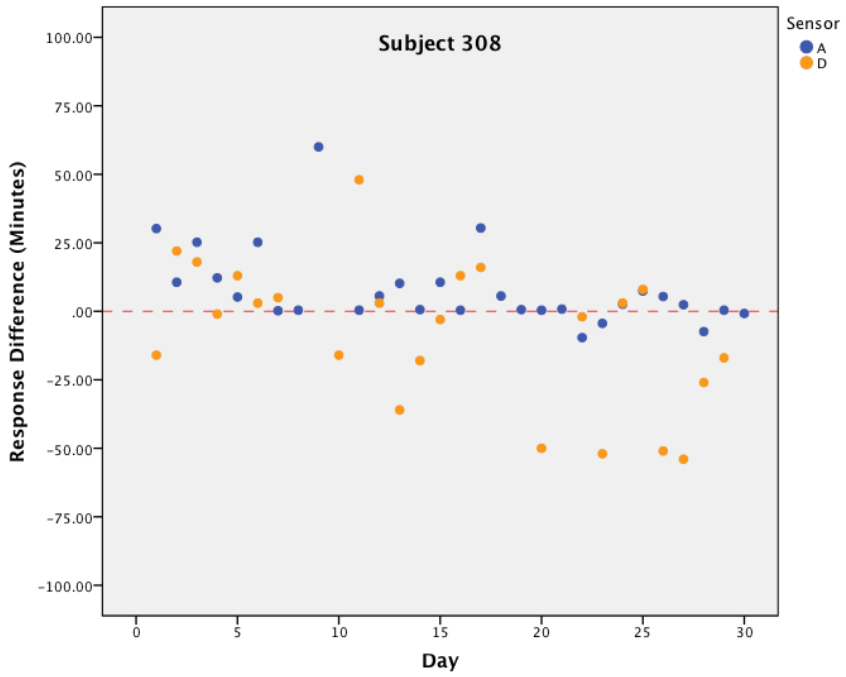
The subject was asked to bring the memory chip from his CPAP unit in for investigation. Unfortunately the subject did not have the memory card in the unit for the whole time he was wearing the appliance; it was only inserted on Day 22 of the trial. Below is a graph, Figure 44, of the amount of leakage from the unit. The median amount of leakage is 15.6 L/minute. In the 95th percentile, the leakage was 34.8 L/minute, with a maximum leakage of 43.2 L/minute.

Figure 44. Graph of the amount of leakage from the subject's CPAP unit



A scatter plot of the response difference of Subject 308 depicting Sensor A and Sensor D revealed that there were a lot data points where Sensor D underestimated wear-time and Sensor A overestimated wear-time (Figure 45).

Figure 45. Response difference of Subject 308 wearing CPAP and OA



Descriptive results on Subject 308 found that Sensor A had a mean absolute response difference of 9.49 ± 12.96 minutes with a median absolute deviation of 5.54 minutes. Sensor D had a mean absolute response difference of 20.58 ± 18.85 minutes. The results are summarized in Table 15.

Table 15. Descriptive results of the absolute response difference (minutes) for the microsensors in subject wearing OA and CPAP

Sensor	n	Mean (95% confidence interval)	Median Absolute Deviation	Mini-mum	Maxi-mum	Standard deviation (SD)	Standard error of mean (SEM)
A	29	9.49 (4.44, 14.35)	5.54	0.20	60.00	13.27	2.46
D	24	20.58 (12.96, 28.20)	16.00	1.00	54.00	18.04	3.68

n= number of observations, with the outliers removed, recorded by the microsensors worn by Subject 308

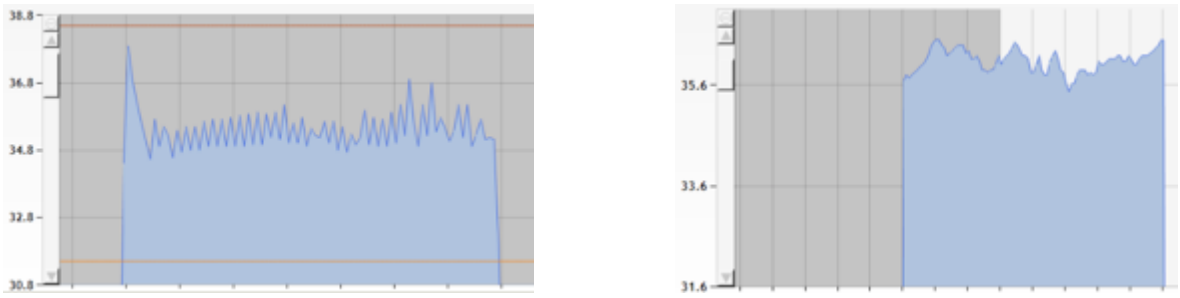
As previously reported, a univariate ANOVA and post hoc Scheffé, with all the subjects included revealed that Subject 308 was statistically different than the other subjects. When Subject 308 was included in the analysis, it was found that there was a significant difference between Sensor A and Sensor D ($p < 0.001$). However, when this subject was removed from the analysis, it was found that there was no difference between the sensor types ($p = 0.45$).

3.4 Anti-deception detection

Sensor A and Sensor T have a "suspicion monitor" built into its software to help clinicians determine if the microsensors are in the mouth or if the data is being falsified. It uses the temperature fluctuations to differentiate the oral environment, which has subtle temperature fluctuations, versus other means of heating, including a water bath. A comparison of the temperature fluctuations seen in the mouth compared to the water bath is depicted in an example of a Sensor A in Figure 46.

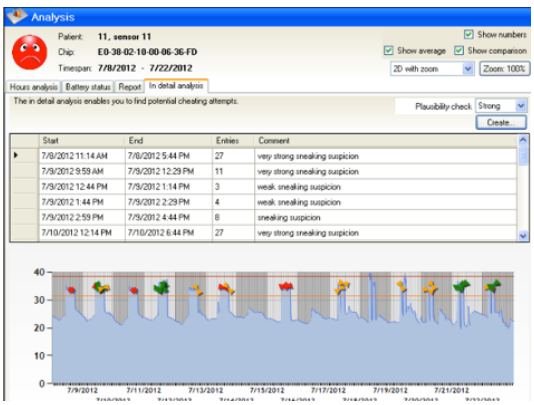
Figure 46. Graph of temperature recordings from Sensor A 230:

A. In the water bath **B. In the mouth**



The software marks sharps peaks and deeps in the temperature as suspicious. The accuracy of "suspicion monitor " is questionable as one can see from a screenshot of Sensor T 011 that was placed in the water bath on July 8-July 22, 2012 (Figure 47). Though the microsensor was placed in the water bath, the monitor reports "very strong sneaking suspicion", "weak sneaking suspicion" and "sneaking suspicion" at specific time points (as indicated by the start and end date and time in the table). These microsensors were placed in the same water bath at the same temperature for all the days, so it is unclear why there would be a difference in the level of suspicious activity. On July 19, 2012, the microsensor was placed in the water bath, as well. However, no suspicious activity was detected on this day as seen by the lack of red, yellow or green arrow on the graph for that date.

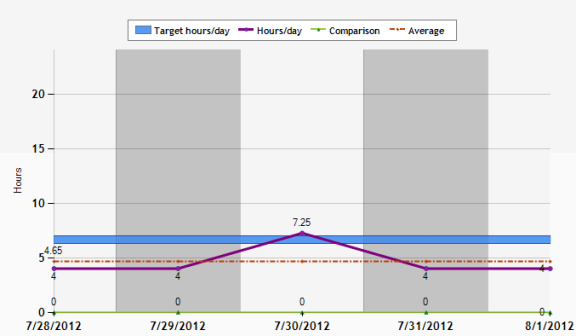
Figure 47. Screenshot of "suspicion monitor" feature of Sensor T



Anti-deception for Sensor D is incorporated into its algorithm, which does not only look at temperature but also head movement to determine wear. For sensor D, the last two columns of its raw data that is collected (*Wearing,* and *Wearing with head position*) were supposed to be zero throughout the data file during phase 1 as the microsensors were in a water bath; thus, no information about wearing or head position from the three-axis accelerometer should have been recorded. This was true except for Tuesday, November 27, 2012 from roughly midnight until 7am (84 observations) on Sensor D301; Thursday, November 22, 2012 and Saturday, January 19, 2013 (91 observations) for Sensor D302; Monday, December 9-12, 2012 and Saturday, January 19, 2013 for sensor D303. On these dates, Sensor D computed an adherence graph even though the microsensor was in a water bath and not in the mouth.

An interesting finding occurred on a day outside of the experimental dates. On July 30, 2012, Sensor T and Sensor A were left in a trunk of a car on a hot summer day. The microsensors were not placed in the mouth or in the water bath that day, yet all of the Sensor T and Sensor A recorded that the microsensors were worn for approximately seven hours that day (example seen in Figure 48). Corresponding temperature graph reveals that this is because the temperature fell within the range considered for "wear" that day. Sensor D was not present when this occurred.

Figure 48. Adherence graph of Sensor T on a hot day



Chapter 4: Discussion

This research is the first non-industry supported study to present bench work testing of three thermosensitive microsensors and *in vivo* testing with quantitative results. Studies using Sensor A and T have not reported statistical analyses on the reliability of the microsensors.[15, 83, 88, 89, 95] Currently, there are no previously published studies on Sensor D, neither *in vitro* nor *in vivo*. With the increased demand for objective adherence monitors, this study will increase our understanding of their accuracy which will support their use in both clinical and research fields.

During phase 1, *in vitro* testing, the microsensors were placed in a water bath and their computed readouts were compared to the logged time of each trial. In the first trial, long durations of "wear" were examined. It was found that Sensor A was the most accurate, followed by Sensor T and then Sensor D. Sensor D had the largest median absolute deviation of five minutes compared to zero deviation of Sensor A and T. In addition, Sensor D was found to overestimate "wear-time" over 80% of the time compared to Sensor A and T who overestimated "wear-time " only 12% and 8%, respectively.

In trial 2, *in vitro* testing, which assessed the microsensors accuracy during short, interrupted durations of "wear", it was found that Sensor A and Sensor T had equal accuracy while Sensor D was significantly different. Sensor D had a median absolute deviation of 10 minutes compared to zero of Sensor A and T. Similar to in trial 1, Sensor D was found to overestimate "wear-time" 70% of the time compared to Sensor A and T who overestimated "wear-time" only 10% and 3%, respectively.

An acceptable threshold of a response difference of the microsensors was established based off the temperature-sensing interval of the microsensors. Sensor A and Sensor D record

temperature every 5 minutes. Sensor T sensing interval is three times that, recording temperature only every 15 minutes. At one time-point within the sensing interval, the microsensor will record if the temperature is within the "wear-time" range; if yes, the software will record that as 5- or 15-minutes worth of appliance wearing which may not be exactly the case. For example, if a patient were to insert their appliance and a minute later remove it, there is a possibility that that time in the mouth will correspond to a microsensors recording time and thus record that time as 5- or 15- minutes in the mouth. However, another microsensor with a slightly different internal clock may not have caught the short time the appliance was in mouth. In addition, the time it takes for the microsensor to cool down from the oral environment may also be a factor. Therefore, if the microsensor is inserted and removed repeatedly from a hot water bath or the mouth, there are an increased number of changes in temperature that the microsensors must detect. Therefore, twice the sensing interval was thought to be an appropriate threshold for the microsensors accuracy.

When the number of deviations that fell outside the threshold was tallied, it was found that Sensor A had more deviations than Sensor T. However, the fact that all the readings of Sensor T fell within the selected twice the sensing interval range should be considered in view of the fact that the sensing interval of this sensor is three times larger than that of the other two sensors. Moreover, the statistical analysis of the absolute deviations from Phase 1 trial 1 and trial 2 identified Sensor A as being either significantly better (trial 1) or not different (trial 2) from Sensor T. Sensor D had the highest number of data points that fell outside twice the sensing interval, specifically in Trial 2. This may be because the of the two temperature changes that occurred in this trial when the sensors were inserted and removed from the water bath twice. It was assumed that the Sensor D recorded wear-time based solely on temperature, which was

incorrect. Sensor D is the only microsensor type to use head movement in its calculations to determine that the device is being worn. Since this feature could not be tested in the water bath, we relied on its temperature recordings to determine if the microsensors recorded "wear". This may explain why Sensor D performed significantly worse than the other two microsensors.

Trial 3, *in vitro* testing, assessed the recording accuracy of the three microsensor typed when they were embedded into different materials. Sensor A and Sensor D showed no significant difference in their recording ability due to three different embedding materials. However, Sensor T had a better recording accuracy for acrylic and thermoactive acrylic than PVC. It is unclear why only Sensor T had a significant difference in recording accuracy with PVC while the other two sensors types did not. However, while statistically this difference is significant, it is not clinically significant. All three materials types used with Sensor T had a median absolute deviation of 0.00 minutes. The mean absolute response differences were 0.67 ± 3.11 minutes, 1.52 ± 6.41 minutes and 3.00 ± 6.03 minutes, for acrylic, thermoactive acrylic and PVC respectively. These differences would not change your clinical decision to choose a specific material over another. While there was no affect due to the material types, Sensor D still overestimated "wear-time" 75% of the time and had a median absolute deviation of 5 minutes, compared to Sensor A and T only overestimated "wear-time" 7% and 8% of the time and had median absolute deviations of zero.

The impact of material type on recording accuracy of microsensors has never been examined in the literature. Previous studies have discussed the concern of using coloured acrylic with microsensors that use optical signals, such as the Smart Retainer, because of the inability for the microsensors to transmit signals through the colour.[87,88] In this study, three clear materials that are commonly used to make removable OA were examined. The three materials have similar

thermal conductivities, *k,* which is defined as the quantity of heat transmitted through a unit thickness in a direction normal to a surface of unit area, due to a unit temperature gradient under steady state conditions. The thermal conductivity of acrylic is 0.2 W/mK, PVC is 0.19 W/m and thermoactive acrylic (Veriflex) is 0.17 W/mK. Since the thermal conductivities of the materials are similar this should not be a factor affecting the recording abilities of the microsensors. However, thickness of the material may have been a factor, while attempts were made by the lab technician to keep the thickness as uniform as possible, it was not standardized between all of the blocks.

While it may have been interesting to examine materials with different thermal conductivities to see if that may be a contributing factor to recording accuracy, these three materials were specifically tested due to their common use in orthodontics and dental sleep medicine treatments. Acrylic is commonly used in orthodontics to make Hawley retainers as well as functional appliances such as twin-block and bionators. Vacuum formed retainers (VFR) are gaining in popularity as a method to retain orthodontic treatment or as a means to correct malocclusions through a series of aligners.[103] The main component of these retainers is made from PVC. Thermoactive acrylic is used in OA for OSA, which allows patients to mold the appliance in hot water for a superior fit upon insertion.[104] The findings of this study are of interest because it demonstrates that the microsensors can be used in different materials. Due to the fact that there was no clinically significant difference found between the materials, it was decided that Phase 2 testing would be conducted using VFR made from PVC. This material was chosen due to the ease of use in fabricating an appliance and the ability to keep the appliance as uniform (in terms of thickness and design) between the subjects. As well, studies have shown the VFR are becoming the most popular retention appliance in orthodontics due their cost-

effectiveness in terms of patient satisfaction, cost, superior clinical outcome and adherence rates.[103, 105, 106]

Phase 2, *in vivo,* testing revealed there was no significant difference between Sensor A and D in their recordings. Sensor A had a lower median absolute deviation of three minutes compared to five minutes of Sensor D. Both sensors types reported zero deviations in wear-time within twice the sensing interval over 80% of the time. Sensor D was found to have the greatest variability and highest frequency of overestimations of "wear-time" in the *in vitro* trials. However, in the *in vivo* phase, it was found that there was no difference in the recording ability of Sensor D compared to Sensor A. This discrepancy may be due to the fact that only raw temperature data from the microsensors were used during the *in vitro* trials to determine "wear-time". This was done because Sensor D's algorithm would not create an adherence graph on the software from the microsensors being in hot water. This is because these microsensors also take into account head movement to determine wear, which is not seen in a static water bath. In the *in vivo* phase, the data examined for both microsensor types, was taken from the graphs tabulated by the software. This was used, rather than the raw data, in an effort to mimic a true clinical setting. The aim was to use the data that the clinicians would see, which would be the formatted adherence graphs and not the raw data. The discrepancy in the findings from Sensor D between Phase 1 and Phase 2 may be due to the fact that only temperature was used as a determinant for wear-time in the *in vitro* trials, which is not a true representation of how these microsensors works. More accurate results on the reliability of these microsensors may be seen in the *in vivo* phase as this took into account temperature and head movement as the microsensors were actually worn by humans and not just in a water bath. Therefore, while it was found that Sensor D had the greatest variability, with a median absolute deviation of 5.00 minutes in Trial 1 and 3

to 10.00 minutes in Trial 2, compared to the other two microsensors, this difference was not seen in the *in vivo* testing, meaning Sensor D can reliably be used in clinical settings.

Using volunteers from the UBC Dental School, in the *in vivo* testing, the aim was to have participants who would be honest and reliable throughout the trial period. Due to the fact that this is the first study to quantitatively examining the reliability of the Sensor A and D in the human oral environment, we did not want to use real patients wearing a removable OA. This is because it is known that patients often misrepresent their true wear-time when asked to keep a log. The purpose of this study was not to examine adherence; rather, the aim was to investigate the reliability of the microsensors. Thus, it was imperative that the logs kept by the subjects were accurate to compare against the recordings from the microsensors. All participants were instructed to be accurate, to the minute, of when they inserted and removed appliance throughout the trial. While, we cannot be sure that subjects were actually as accurate as they were instructed to be, because no statistical difference was found between the subjects' logs and microsensors' records (which the participants were not able to see), we can conclude that that Sensor A and Sensor D can reliably record wear-times in the oral environment.

When the cumulative amount of time that the sensors deviated from the sensing interval was determined, it was found that both microsensors had an overall error of less than 2%. Out of the cumulative logged time of 108 days, there was a deviation of only 2 days. This most likely will not impact a patient's treatment. The overall error is very small and is not clinically significant as the recommended usage of removable appliances is typically daily or nightly usage over a period of approximately 12 months or longer, depending on the treatment. Proffit[107] recommends patients undergoing growth modification using removable functional appliances should be wearing the appliances nightly for approximately 12 hours per day for 10-12 months.

Graber recommends 20 hours/day wear of Class III functional appliances such as the Frankel-3.[108] Headgears and facemask are prescribed to be worn for 12-14 hours/day for 12-18 months.[107, 108] Post orthodontic treatment retainers are recommended to be worn full time, except while eating, for 3-4 months and then on a part time basis, usually nightly, for 12 more months.[107] Aligners, such as those used with Invisalign treatment, are to be worn by patients for 20-22 hours/day for treatment that can take anywhere from 3-12 months or longer.[108, 109] Patients treated for OSA with CPAP or OA are generally described as being adherent if they wear their appliances for 4 hours/night.[9-11, 15] Since such treatment is not curative, patients may be using such devices indefinitely. As such, an overall error of less than 2% would not make a large impact on a patient's treatment outcomes.

To date, there are no peer-reviewed studies on the *in vivo* accuracy of Sensor A and D. As previously reported, Sensor A uses the same software as Sensor T. In a study by Pauls et al,[89] they reported a discrepancy of 7.92 minutes with Sensor T but no statistical analysis was done as their sample size was one. Schott et al[44] reported high reliability of Sensor T as over a 15-month period the microsensors recorded temperatures daily at 15-minute intervals for all 100 participants in the study. They stated that this represented exceptional performance of the device, yet no investigation was done into whether or not the recordings were accurate. Vanderveken et al[15] study, which also used Sensor T, reported no significant difference in the objective measured wear-time compared to the subjective log of subjects. The median self-reported adherence rate in the first month of the trial was 7.34 hours/day compared to the median objective adherence rate of 7.24 hours/day. The difference is 0.1 hours/day or 6 minutes/day. In the second and third months of the trial it was found that the median self-reported adherence was 7.21 hours/day compared to the median objective adherence rate of 7.13 hours/day. This is a difference of 0.08

hours/day or 4.8 minutes/day.[15] This study is in agreement with our current findings that although there are some small differences in the computed values compared to self-reported adherence rates, they are not clinically significant and a 10 minutes difference in their precision would not impact treatment outcomes.

As a quality control trial to assess for false positives, the microsensors were left out of the water baths for 30 days. No effort was made to ensure that the room temperature was kept below 31.5 ^{0}C. While the probability of the microsensors reporting false positives was very low and all three microsensors were found to be highly specific, there is a possibility that the microsensors may be recording if there was an increase in temperature in the room (i.e. if it was a hot day outside). It was noted that the outside temperature does impact the microsensor readings, which was seen when Sensor A and Sensor T recorded "wear-times" when left in a car on a hot summer day. Therefore, clinicians may want to consider asking patients to store their oral appliances in cold water in a container when they are not wearing them. This will limit the number of false positive, which may occur if the appliance is left by the window or in a hot, steamy bathroom.

In addition, it is important to note that 3/25 (12%) Sensor D microsensors were faulty, including one microsensors with an improper calendar and two microsensors whose batteries died prematurely. There were no microsensors from Sensor A or Sensor T types that had to be excluded for technical reasons. Vanderveken et al[15] reported unspecified technical difficulties with 1/51 (1.96%) Sensor T microsensor over their 3-month trial. Schott et al[44] reported no technical difficulties in 100 Sensor T microsensors over 15-month trial. There was no mention of technical difficulties in the study by Pauls et al[89] with 14 participants wearing appliances with Sensor T over 168 days. When this study began Sensor D was still undergoing beta testing with its manufacturer. This may explain why there was an increase number of Sensor D microsensors

that failed. It is important to ensure high quality control testing from the manufacturer to ensure that clinicians do not receive faulty microsensors that may die prematurely. All three of the microsensors are completely embedded in acrylic, as per manufacturers' instructions, to attach them the oral appliances. As such, they are very difficult to remove and replace. The manufacturers warn about using high heat acrylic burs close to the microsensors. Therefore, it is imperative that the manufacturers ensure proper testing of each microsensors before they are shipped out to clinicians, as it is not easy to remove or replace faulty sensors.

4.1 Case Report

Further investigation was done into one of the subjects who participated in the *in vivo* testing of the microsensors who wore a CPAP unit while wearing the OA with the embedded microsensors. While, CPAP is often the primary choice for the treatment of OSA, for numerous reasons, patients cannot always tolerate the use of CPAP. Mandibular advancement device therapy is an increasingly popular alternative. As well there is literature that recommends combined CPAP and MAD therapy. A case report was published of a 61-year-old male patient with OSA who had difficulty finding the optimal CPAP pressure to control his obstructive sleep events and so he was prescribed combination therapy of CPAP and MAD. The report states that the combined therapy helped improve his sleep, his daytime sleepiness decreased significantly and AHI decreased.[110] El-Solh et al[111] conducted the first prospective pilot study on the combined OA and CPAP therapy for OSA. Ten patients with residual apnea/hypopnea events on MAD who were intolerant to CPAP were recruited. Subjects were asked to wear their MAD along with CPAP for three consecutive nights. The results found that the combination of therapies, compared to a single modality therapy, reduced the number of obstructive events, the

residual AHI was decreased, the number of oxygen desaturations decreased and daytime sleepiness decreased. The authors concluded that the combination therapy is effective in normalizing respiratory disturbances in patients who are intolerant to CPAP alone.[111] While the mechanisms are still unknown, one explanation may be that MAD improves the patency of the velopharyngeal segment of the upper airway, which would mean that the CPAP does not need as much pressure to maintain patency.[110, 111] Further research is needed with increased number of patients, longer testing periods and varying degrees of OSA to determine the indications, benefits and risks of this combination therapy. Nevertheless, with combination therapy being prescribed to patients, it is of interest to know if these microsensors would be reliable in such circumstances.

The microsensors tested primarily work through temperature detection. It was found that subject 308 recordings were significantly different than the other subjects. While it is difficult to statistically analyze the data from only one subject, observation revealed that Sensor D tended to underestimate wear-time for this subject. From the raw data analysis of the microsensors it was seen that the temperature recorded in the mouth often dropped below the temperature threshold of Sensor D. Sensor A, had a lower temperature threshold; thus, the intraoral temperature was recorded above this lower limit while the OA was being worn, which is why the log from Sensor A more closely matched the adherence graph of Sensor A. It is possible, that due to the airflow from the CPAP unit, that there was a lower intraoral temperature if this patient slept with his mouth open without a tight lip seal around the OA. The increased amount of leakage seen from the CPAP unit recordings may be what is causing the temperature in the mouth to drop. There may be positive pressure creating a path of cool air that circulates around the microsensors.

While the increase airflow in the mouth is a plausible explanation for the discrepancies seen, it needs further investigation to understand its true reasons.

By examining only one case of a subject wearing a CPAP with the OA, it is impossible to determine if the statistical significant difference found can be attributed to the combination therapy. This case report draws our attention to the need for further investigations to determine if these microsensors can be used in OA while patients are concurrently using CPAP. More investigations needs to be done to determine the following questions: is the temperature in the mouth lower than average if a patient is wearing CPAP, does the amount of leak from the CPAP unit impact the oral temperature and does breathing with your mouth open while wearing a CPAP impact the accuracy of the microsensors. It may be appropriate to lower the temperature threshold of the microsensors or chose a microsensor with a lower temperature threshold if prescribing combination therapy. Further studies need to be done to determine what an appropriate temperature cut-off would need to be.

4.2 Anti-deception detection

A full statistical investigation into the anti-deception feature of the microsensors was not conducted. However, it was observed that there were several flaws in the microsensors ability to detect if the microsensors were in the water bath compared to the mouth. The "suspicion monitor", which is a feature of Sensor T and Sensor A, is hard to use and difficult to navigate because it relies on the clinician to ask the software if there is any suspicious activity and on what day. The software does not automatically alert the clinician. The software still includes all data, even if suspicious, into its calculation of wear-time and is displayed in the adherence graphs. It is unclear why the monitors did not pick up that the microsensors were in a

"suspicious" environment throughout phase 1 testing. In addition, when Sensor A and T where left in a car on a hot day, they recorded that the microsensors were being worn. Therefore, while an anti-deception feature is a nice additional feature to have, the accuracy of the "suspicion monitor" requires further examination before clinicians can trust it with their patients.

Sensor D, which according to the manufacturers is not supposed to produce an adherence graph at all when the microsensors are not in the mouth, did on several dates. It is not clear why this occurred because the microsensors were static in the water bath and the three-axis accelerometer should not have recorded any movement. For the most part, no adherence graphs were produced for Sensor D during phase 1. Thus, it seems it would be much harder for patients to deceive and falsify wear-time with Sensor D compared to Sensor A and T. It may be advisable to tell patients to store their appliances with embedded microsensors in a cool location, out of sunlight and clean the appliance with cold water to avoid increased temperature recording that may be calculated as wear-time.

4.3 Limitations of the study design

The basic design of this study was based on the methods by Schotts and Goz,[90] who used a water bath to replicate the oral environment. While there are several limitations to the use of the water bath, it is thought to be an accurate way to mimic the oral environment's temperature to test the thermosensitive microsensors. An improvement was made in this study compared to the study by Schotts and Goz[90]; in this study, the microsensors were only placed into the water bath once the desired temperature of 35 ^{0}C was reached and stable. This was done by turning on the water bath for at least one hour prior to the experiment and allowing the temperature fluctuations to stabilize prior to inserting the microsensors. The temperature was verified using a

mercury thermometer. A thermocouple connected to the water bath would have been a more accurate way to monitor the temperature in the water bath throughout the trials. In the study published by Schotts and Goz,[90] the microsensors were always in the water bath and a timer was used to turn the water bath on and off. This method is disadvantageous in that one cannot take into account how long it took for the water bath to heat up to the desired temperature or cool off. As well, it was seen from assessing the water bath's temperature every 15-30 minutes for three hours that the temperature in the water bath fluctuated greatly in the beginning but the temperature became more stable after the first hour. As such, the design of this study allowed the water bath to heat to the desired temperature and stabilize before the microsensors were added. A static water bath did not activate the three-axis accelerometer that is used by Sensor D to determine wear. Incorporating a vibrating plate may have may have provided more accurate recordings for Sensor D in the *in vitro* trials.

Phase 1 testing of the three types of microsensors involved a small sample size of each sensor (Sensor A, n = 30; Sensor T, n = 20; Sensor D, n = 16). The relatively small and uneven number of microsensors tested was because we were dependent on industry donations of the microsensors. Sensor D, at the start of the trial, was still undergoing beta testing phase and we could not obtain an increased number of microsensors to match Sensor A and T. No previous studies could be used as a basis to determine an appropriate sample size. However, despite the small sample number, because each microsensor was tested in each trial for 30 days, the sample size (n) is actually much larger, ranging from 90 to 840, depending on the trial. Phase 2, *in vivo* testing, was conducted with 14 volunteers. However, again because each of the microsensors was used to generate repeated measures over the 30-day trial, the sample size used in the analysis was over 360. Only one previous study, which had a sample size of one, over a 2-week period, has

attempted to assess the accuracy of Sensor T *in vivo*.[89] There are no other studies on the accuracy of Sensor A or D with *in vivo* testing. This pilot study can now be used as the basis for future studies with patients. Lastly, if the number of data points had shown the need for further analysis, we would have asked for more microsensors from the manufacturers. However, we found that with our methodology our sample size was sufficient to test our hypotheses.

Blocks of material with embedded microsensors were used for trial 3 of *in vitro* testing. It was not possible to embedded the microsensors completely in PVC or thermoactive acrylic because the high temperature needed to form these materials would destroy the microsensor. Thus, a thin flat bottom layer of the specific material was used and the microsensor was then covered with acrylic. Therefore, all 3 types of blocks included an acrylic covering. Nevertheless, this trial was designed to mimic real-life settings where the microsensors would have to be attached to an OA, made of any material, by covering it with acrylic. The design of the blocks is reflective of the clinical application of the microsensors. In addition, it was difficult to embedded the microsensors in the material of equal thickness. While the same laboratory and technician were used to fabricate all of the blocks, it was not possible to ensure that they were all of equal thickness though this attempt was made. However, the results of this study found that there was no clinical significant difference in the recording ability of the three types of microsensors in the three materials. This demonstrated that the thickness of the material was not a confounding factor.

4.4 Advantages and disadvantages of sensor types

The results of this study indicate that clinicians can chose any of the three thermosensitive microsensor types to use in removable OA. All three were shown to be clinically

reliable in determining “wear-time”. Therefore, clinicians will have to choose which microsensor to use based on other features, which may prove one microsensor type to be more advantageous over another in certain clinical situations. The decision as to which microsensor to use will be based more so on which software does the clinician prefer, which adherence graph is easier to read off, which microsensor has a faster read off time and cost. Table 16 summarizes the author’s opinion of the main advantages, disadvantages and key features of the three microsensors.

Table 1. Summary of advantages and disadvantages of each sensor

Sensor	Advantages	Disadvantages
Sensor T	- Easy to use reader- reader has no problem locating microsensor - Date cut off is midnight-to-midnight which is more appropriate for day time wear OA (Sensor T is marketed for orthodontic appliances) - Storage of 100 days - 0/30 microsensors were faulty	- Longest interval in recording temperature (15 minutes) - Only uses temperature as basis for determining wear-time - Large temperature range with really low lower temperature limit (31.5-38.5 ^{0}C) - "Suspicious activity" feature is difficult to use - Easy to falsify- can place in hot water, under hot locations, etc. - The greater the length of time between the data being read off by the software, the longer the read out process can take
Sensor A	- Easy to use reader- reader does not have a problem picking up and locating microsensor - Short interval of recording time (5 minutes) - 0/20 microsensors were faulty	- Only uses temperature as basis for determining wear-time - Large temperature range with really low lower temperature limit (31.5-38.5 ^{0}C) - "Suspicious activity" feature is difficult to use - Easy to falsify- can place in hot water, under hot laps, etc. - The greater the length of time between the data being read off by the software, the longer the read out process can take - Date cut off is midnight-to-midnight which is more difficult to interpret for night time wear of OA (Sensor A is marketed for OSA appliances) - Storage only for 30 days- patient needs to come in more frequently to have data read off
Sensor D	- 3-axis accelerometer which can determine head position and sleeping position - Short interval of recording time (5 minutes) - Narrower temperature range more reflective of oral environment temperature (33.5-39.2 ^{0}C) - Graph depicts exactly what time the OA was worn/removed each day - Date cut off is noon-to-noon, which is easier to read to determine night-time wear pattern (Sensor D is marketed for OSA appliances) - Read off time is always <1minute - Harder to falsify- wear is not solely based on temperature - Longest storage time of 180 days	- More difficult to position the microsensor in the reader station to have the data read off - Statistically, *in vitro,* tends to over-estimate wear-time and has the largest variability which may not be of clinical significance - 3/25 microsensors were faulty

4.5 Future studies

Future studies are needed to assess patients wearing patterns of OAs as part of orthodontic treatment and for sleep therapy. These microsensors should be incorporated into future studies assessing the effectiveness and efficiency of OAs, thereby eliminating the subjective bias of measuring adherence with self-reports. Randomized control trials, similar to the one done by Philips et al,[112] should incorporate the microsensors when comparing the CPAP therapy to OA therapy. These objective adherence monitors may also help investigators examine the issues of adherence and help to determine if there is a true predictor of patient behaviour that will help clinicians assess patient adherence.

Other variables that should be tested that may impact accuracy of the microsensors include the position in which they are embedded into the OA. In this study, both sensors were embedded onto the buccal shelves of the maxillary appliance. It is unknown if the sensors would be able to record as reliably if the sensors were embedded onto the palatal area. It is possible that the temperatures in the palatal area of the oral cavity would be lower than in the buccal region, as the microsensor would not be in close contact with the cheek. If this is true, the microsensors may not record these lower temperatures. This may also be a concern for patients who are mouth breathers. Instructions for embedding Sensor D into an OA recommended placing the sensor in the mandibular arch if using with a functional appliance. This position was not tested by this study. Therefore, future investigations should examine whether or not positioning in the OA effects reliability of the microsensors. In addition, as previously mentioned, future studies should examine the reliability of the microsensors when OAs are used in conjunction with CPAP for combination therapy. Sensor D's feature, which records head movement and position, was not

examined in this study. Future studies are needed to determine the accuracy of this accelerometer in determining head position.

The longevity of the microsensors was not examined in this study. Manufactures report a battery life of greater than 18 months for Sensor T and A and greater than 24 months for Sensor D. The microsensors were used for 4 months, one month each for trial 1, trial 2, control trial and *in vivo* testing. This was completed over the span of one year (July 2012 to July 2013). It is unknown if the microsensors decrease in accuracy over time or how long the battery lasts in a real-life setting. Longer trials with these microsensors would help answer this question. It is important to understand the longevity of these microsensors so that clinicians should know what to expect and when the microsensors need to be replaced.

Microsensor technology has improved greatly over the past several decades. With new features, smaller size and excellent reliability, these microsensors will change the way clinicians monitor adherence. While further testing of these microsensors is warranted, especially in real-life settings, this study can serve as a platform for future research in the field. In the future, it would be ideal if the microsensors had the capacity to send the information to clinicians even if patients are not coming to the office. This wireless transmission is available for some CPAP units and may be the future for the field of OA adherence monitors. This is likely more challenging as the microsensors need to be small enough to not be uncomfortable to patients and the wireless transmission needs to be proven safe to do while the microsensors are in the mouth. With improvements in technology, the clinical possibilities are extensive. This study is an important stepping-stone to understanding how these adherence monitors work and their accuracy. It will provide the foundation for future research using these microsensors.

Chapter 5: Conclusion

The research presented in this thesis has examined three microsensors that are currently being marketed to clinicians as adherence monitors for removable OA. The results demonstrated that all three microsensors may be used in clinical settings to help clinicians monitor adherence with removable OA. *In vitro* testing, using a water bath, found that Sensor D tended to have the largest deviations in its recordings compared to Sensor A and Sensor T. However, in the *in vivo* phase, Sensor A and D were found to have similar accuracy. Clinically, there are no significant differences in terms on material type on the recording accuracy of the microsensors. All three microsensors are highly specific and over a 30-day period had an overall error of less than 2% in its recording accuracies.

The implication of the use of these monitors in future studies as a reliable measure of adherence and their impact on treatments outcomes may change practice protocols for both orthodontists and dental sleep medicine clinicians. With these objective adherence monitors, clinicians will have an objective and accurate measure of their patients' appliance wearing routines. The computed adherence graphs can be used to provide feedback to patients to help them improve their adherence. The literature has shown that adherence rates are due to multifactorial influences because of the nature of human behaviour.[1, 18, 32, 35] Thus, clinicians no longer have to predict which patients will be adherent or not with removable OA therapy.

In addition, the advent of these microsensors is critical for evidence-based research in the field of dentistry and sleep medicine. The need to objectively monitor patient adherence in these trials is essential to limiting subjective bias. Microsensors will help clinicians compare the

effectiveness and efficiency of various devices. These microsensors have a huge implication in clinical research and will greatly improve the level of evidence in dentistry.

Microsensor technology is a new and exciting addition to orthodontics and dental sleep medicine. This is the first study with statistical analyses to corroborate reports that these thermosensitive microsensors are reliable and can be use to determine wear-time of removable OAs.

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Appendix A. Participation information and consent form

Title of the study: "Evaluation of microsensor technology to monitor adherence with removable orthodontic retainers and oral appliances for sleep apnea"

Principal Investigator: Dr. F.R. Almeida, DDS, MSc, PhD
Department of Oral Health Sciences
UBC Faculty of Dentistry
Telephone (XXX) XXX-XXXX

Co-Investigator(s): Dr. S.J. Kirshenblatt, BA, DDS
Graduate Orthodontics
UBC Faculty of Dentistry
Telephone (XXX) XXX-XXXX

Dr. H. Chen, DMD, MSc, PHD
Department of Oral Health Sciences
UBC Faculty of Dentistry
Telephone (XXX) XXX-XXXX

Sponsor: This research not being sponsored

Emergency Telephone Number: Dr. Almeida – (XXX) XXX-XXXX or Dr. Kirshenblatt – (XXX) XXX-XXXX

1. INVITATION

You are being invited to take part in this research study because we are conducting a pilot study to gather information on the accuracy of microsensors in removable appliances and require volunteers who will be honest and thorough throughout the trial period so that we can use this data before testing the microsensors on orthodontic and sleep apnea patients. As a dental student we have confidence that you will be reliable and accurate in the reporting of the usage of microsensors. Because of your knowledge and understanding of the dental field, we have invited you to participate in this pilot study.

2. YOUR PARTICIPATION IS VOLUNTARY

Your participation is voluntary. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time without any negative consequences to your class standing and grades.

Before you decide, it is important for you to understand what the research involves. This consent form will tell you about the study, why the research is being done, what will happen to you during the study and the possible benefits, risks and discomforts. You also need to know that

there are important differences between being in a research study and being cared for by your doctor. When you participate in a research study, the main goal is to learn things to help other patients in the future. Outside a research study, your doctor's sole goal is to care for your health. Nevertheless, the researchers have a duty of care to all subjects and will inform you of any information that may affect your willingness to remain in the study.

If you wish to participate in this study, you will be asked to sign this form.

Please take time to read the following information carefully and to discuss it with your family and friends before you decide.

3. WHO IS CONDUCTING THE STUDY?

This research study is being conducted as part of Dr. S.J. Kirshenblatt's Master's thesis in Craniofacial Science at UBC Faculty of Dentistry Graduate Orthodontics program.

The study is not receiving funds from an external agency or sponsor.

4. BACKGROUND

Successful orthodontic treatment with removable appliances is impossible without good patient compliance. Several studies have attempted to monitor patient compliance in an objective manner by using microsensors; however, the majority have used the sensors extraorally in appliances such as headgears. Until recently, the technology to manufacture a small microsensor that could be incorporated into an intraoral appliance and withstand the oral environment has not been practical nor commercially available. With improvements in objective monitoring capability, orthodontists will be able to track patient compliance, motivate patients, and improve research methods by having an objective wear-time measure for removable appliances. In addition, the incorporation of such monitors into appliances used for obstructive sleep apnea (OSA), will allow practitioners to evaluate the effectiveness of OAs, such has mandibular advancement devices. One of the key gaps in research of OSA, as outlined by Agency for Healthcare Research and Quality in February 2012, is that there are no studies that have evaluated the predictors of compliances with OA and trials addressing compliances have only been objectively done for continuous positive airway pressure (CPAP) treatment. A small microsensor that can be embedded into OA would allow for direct comparison of compliance rates with different interventions and incorporation of compliance into an overall comparison of effective treatment. This study will evaluate the reliability of microsensors, which will have important implications for their use in future research.

5. WHAT IS THE PURPOSE OF THE STUDY?

The purpose of this study is to evaluate the *in vivo* reliability of two small radio-frequency microsensors embedded into an oral appliance. We would like to test how the microsensors can be embedded into oral appliances, any differences between the two types, and how they compare to a log kept by participants.

Feasibility Study or Pilot Study
Before proceeding to a full-scale study, a ”pilot study” or “feasibility study” is often carried out first to test the design of a study, the likelihood of successful recruitment or the acceptability of the intervention to potential subjects. The basic idea is to find out if it will be useful to commit the resources to proceed to a potentially definitive study. The “design” of a study is how the study will be done, how the data are collected, whether that data can provide useful information and whether it will be practical to proceed to a larger study that will include more subjects. This type of study involves only a small number of subjects and therefore the results can only be used as a guide for further larger studies. There is no guarantee that a larger study will be done and it is not expected that you will benefit from taking part in this study (or that you will be part of a future larger study if it is done), although the knowledge gained may help to develop future studies that may benefit others.

6. WHO CAN PARTICIPATE IN THIS STUDY?
You may be able to participate in this study if you have*:*

- Undergraduate or graduate dental student at UBC
- Complete dentition (excluding wisdom teeth)
- No missing teeth
- No active dental decay
- No active periodontal disease
- No cleft lip/palate
- No oral pathology

7. WHO SHOULD NOT PARTICIPATE IN THE STUDY?
You should not participate in this study if you feel that you cannot wear an oral appliance at night for whatever reason (i.e. claustrophobia).

8. WHAT DOES THE STUDY INVOLVE?
The study involves having an oral appliance fabricated for your mouth and microsensor will be embedded into the side of the appliance. You will have to wear to appliance at night and record in a log as to when the appliance is inserted and removed each night. You will be asked to complete a questionnaire about demographics and the comfort of the appliance. All visits will take place at UBC Faculty of Dentistry Clinic.

If You Decide to Join This Study: Specific Procedures
Screening:
The first visit will be an intraoral screening to ensure that you are not missing any teeth and a quick check to ensure you have no obvious signs of active decay or periodontal disease. This screening will ensure that there will be no harm if you were to wear an appliance on your dentition at night. If you pass the screening, an impression of the maxillary dentition will be taken for fabrication of the appliance.

Trial:
If you agree to take part in this study, the procedures and visits you can expect will include the following: you will be fitted with an oral appliance with an embedded microsensor. Adjustments can be made to the appliance at this point to ensure your comfort while wearing the device. You

will be asked to wear the appliance at night for a minimum of 5 hours for 1 month. You will need to keep a log of the exact time that you put the appliance in at night and removed it in the morning. The amount of time the appliance is worn from night to night may vary. The importance is that you accurate record when you insert and remove the appliance. Every 15 days you will need to return to the dental clinic at UBC Faculty of Dentistry to have the microsensor read and checked. The total number of visits will be 4, each 15 minutes (2 visits to make the appliance and 2 visit throughout the treatment time to read the microsensor). Your participation in this study will not conflict with your class time. Photographs may be taken to demonstrate the design of the appliance and placement of the microsensor intraorally.

9. WHAT ARE MY RESPONSIBILITIES?
If at any point during the trial, if you find that you are unable to wear the appliance or are feeling any discomfort or changes in your dentition, it is your responsibility to call Dr. Kirshenblatt to inform her of this change.

10. WHAT ARE THE POSSIBLE HARMS AND DISCOMFORTS?
There are no potential risks to participating in this study. You may experience some discomfort from the appliances.

11. WHAT ARE THE POTENTIAL BENEFITS OF PARTICIPATING?
No one knows whether or not you will benefit from this study. There may or may not be direct benefits to you from taking part in this study.
We hope that the information learned from this study can be used in the future to benefit other people with a similar disease.

12. WHAT ARE THE ALTERNATIVES TO THE STUDY TREATMENT?
There is no alternative to the study treatment. If you choose to not participate in this study that is up to your discretion, however, there is no alternative study you can participate in.

13. WHAT IF NEW INFORMATION BECOMES AVAILABLE THAT MAY AFFECT MY DECISION TO PARTICIPATE?
If you choose to enter this study and at a later date a more effective treatment becomes available, it will be discussed with you. You will also be advised of any new information that becomes available that may affect your willingness to remain in this study.

14. WHAT HAPPENS IF I DECIDE TO WITHDRAW MY CONSENT TO PARTICIPATE?
You may withdraw from this study at any time without giving reasons. If you choose to enter the study and then decide to withdraw at a later time, all data collected about you during your enrolment in the study will be retained for analysis. It is a legal requirement that these data cannot be destroyed.

15. CAN I BE ASKED TO LEAVE THE STUDY?
If you are not able to follow the requirements of the study or for any other reason, the study doctor may withdraw you from the study. On receiving new information about the treatment,

your research doctor might consider it to be in your best interests to withdraw you from the study without your consent if they judge that it would be better for your health.

16. WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?
Your confidentiality will be respected. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law.

You will be assigned a unique study number as a subject in this study. Only this number will be used on any research-related information collected about you during the course of this study, so that your identity [i.e. your name or any other information that could identify you] as a subject in this study will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to insure that your privacy is respected and also give you the right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor.

Your birth date will also be provided if requested by the responsible regulatory agency.

Disclosure of Race/Ethnicity
Studies involving humans now routinely collect information on race and ethnic origin as well as other characteristics of individuals because these characteristics may influence how people respond to different medications. Providing information on your race or ethnic origin is voluntary.

17. AFTER THE STUDY IS FINISHED
You and other patients may not be able to receive the study treatment after your participation in the study is completed. There are several possible reasons for this, some of which include: The treatment may not turn out to be effective or safe. The treatment may not be approved for use in Canada. It may be too expensive and insurance coverage may not be available. The treatment, even if approved in Canada, may not be available free of charge.

18. WHAT HAPPENS IF SOMETHING GOES WRONG?
Signing this consent form in no way limits your legal rights against the sponsor, investigators, or anyone else, and you do not release the study doctors or participating institutions from their legal and professional responsibilities.

In case of a serious medical event, please report to an emergency room and inform them that you are participating in a clinical study and that the following person can then be contacted for further information: Dr. Almieda at telephone number: (XXX) XXX-XXXX

19. WHAT WILL THE STUDY COST ME?

Reimbursement*:* there will be no reimbursement for study related expenses.

Remuneration: you will be not paid for your participation in this study .

20. WHO DO I CONTACT IF I HAVE QUESTIONS ABOUT THE STUDY DURING MY PARTICIPATION?

If you have any questions or desire further information about this study before or during participation, or if you experience any adverse effects, you can contact Dr. Almeida or Dr. Kirshenblatt.

21. WHO DO I CONTACT IF I HAVE ANY QUESTIONS OR CONCERNS ABOUT MY RIGHTS AS A SUBJECT?

If you have any concerns or complaints about your rights as a research subject and/or your experiences while participating in this study, contact the Research Subject Information Line in the University of British Columbia Office of Research Services by e-mail or by phone.

22. SUBJECT CONSENT TO PARTICIPATE

Title of the study: "Evaluation of microsensor technology to monitor adherence with removable orthodontic retainers and oral appliances for sleep apnea"

23. SIGNATURES

Subject Consent

My signature on this consent form means:

- I have read and understood the subject information and consent form.
- I have had sufficient time to consider the information provided and to ask for advice if necessary.
- I have had the opportunity to ask questions and have had satisfactory responses to my questions.
- I understand that all of the information collected will be kept confidential and that the results will only be used for scientific objectives.
- I understand that my participation in this study is voluntary and that I am completely free to refuse to participate or to withdraw from this study at any time without changing in any way the quality of care that I receive.
- I understand that I am not waiving any of my legal rights as a result of signing this consent form.
- I understand that there is no guarantee that this study will provide any benefits to *me*

I will receive a signed copy of this consent form for my own records.

I consent to participate in this study.

_____	_____	_____
Subject's Signature	Printed name	Date

_____	_____	_____	_____
Signature of Person Obtaining Consent	Printed name	Study Role	Date

Appendix B. Subject log

LOG OF APPLIANCE WEAR Subject N[0:]

Day	Date	Time inserted (___:___AM/PM)	Time removed (___:___AM/PM)	Describe any problems, concerns, discomfort, if any. Did you drink/eat while wearing appliance?*
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				
21				
22				
23				
24				
25				
26				
27				
28				
29				
30				

- Please do NOT eat or drink while wearing the appliance, Rinse with COLD water after removal to clean appliance

Appendix C. Subject questionnaire

Evaluation of microsensor technology to monitor adherence with removable orthodontic retainers and oral appliances for sleep apnea

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Subject N^0: _____

Circle: Male/Female

Birthdate: ____ / _____ / _____ (dd/mm/yyyy)

Please answer yes (Y) or no (N):

1. Do you breath through your mouth during the day? _____
2. Do you have dry mouth in the morning after sleeping? _____
3. Do you snore? _____
4. Do you grind your teeth at night? _____
5. Have you ever worn an oral appliance before? _____
    a. Describe type (ie. Retainer, functional appliance, night guard, oral appliance for sleep apnea)

       _____
6. How long do you usually sleep at night? (hours) _____
7. Do you have any respiratory problems? (i.e. asthma, seasonal allergies, etc)

   Describe:_____

   _____

Appendix D. Microsensors showing discrepancy of time compared to log in quality assessment

Sensor Type	Sensor Number	Date	Log Time	Sensor Time
A	205	2013-02-15	0	5
A	205	2013-02-16	0	25
A	206	2013-02-16	0	20
A	207	2013-02-15	0	15
A	207	2013-02-16	0	30
A	217	2013-02-16	0	25
A	223	2013-02-16	0	10
A	224	2013-02-16	0	15
A	226	2013-02-16	0	15
T	105	2013-02-16	0	15
T	106	2013-02-16	0	15
T	116	2013-02-16	0	15
T	117	2013-02-16	0	15
T	120	2013-02-16	0	15
D	310	2013-02-16	0	10
D	311	2013-02-16	0	15
D	317	2013-02-12	0	120
D	317	2013-02-16	0	135
D	317	2013-02-21	0	120
D	317	2013-02-24	0	120
D	317	2013-02-28	0	120
D	317	2013-03-03	0	120
D	317	2013-03-07	0	245
D	320	2013-02-16	0	15
D	321	2013-02-16	0	10
D	324	2013-02-16	0	15
D	325	2013-02-16	0	5