Ira R. Casson MD - Written Statement - January 4, 2010

I want to thank the chairman and the other members of the committee for inviting me to participate in this hearing. I will directly address the issue in question, namely, whether or not a career in professional football causes long term chronic brain damage. The media has consistently misrepresented my position by reporting that I deny the possibility that professional football may be the cause of long term brain damage. That is not my position. My position is that there is not enough valid, reliable or objective scientific evidence at present to determine whether or not repeat head impacts in professional football result in long term brain damage. I believe that there is tau pathology in the brains of some retired professional football players and that a number of retired NFL players have legitimate neurological and behavioral/psychological symptoms. As a physician I am very concerned about the possible long term implications of these findings regarding the health and safety of NFL players. I sympathize with the players and the families who are affected.

As physicians and scientists, it behooves us to critically evaluate the evidence before reaching definitive conclusions. My education, training and clinical experience have provided me with the tools necessary to accomplish this task. In the process of researching and writing my honor's thesis at Cornell, I learned how to critically analyze scientific manuscripts and how to view science in its historical and social contexts. I studied how political pressures can subvert the scientific process. During my medical school years at NYU, I learned how to transfer information gleaned from scientific research to the clinical evaluation and treatment of patients. As resident and chief resident in neurology at NYU-Bellevue, I was fortunate to have had the unique experience for a neurologist of having primary clinical responsibility for the diagnosis and treatment of many hundreds of patients with head injuries of all severities. After completing my residency, I pursued my clinical interest in head injuries

by studying boxers. Over the next few years, I exhaustively studied the neurological literature regarding brain injuries in boxers and performed numerous neurological examinations of boxers. With the assistance of many colleagues, I performed clinical neurological research studies on active and retired boxers. Our study on retired boxers that was published in JAMA was the first to report the results of clinical neurological examinations, neuropsychological testing, EEGs and CAT scans of the brain in retired boxers. The evidence collected in that study demonstrated that modern era retired boxers had signs of chronic brain damage. Many in the boxing community expressed their displeasure with the findings and criticized the paper. This did not deter me from publication. Then, as now, my allegiance was to scientific truth and I followed the scientific evidence.

Since 1982, I have been in solo private practice of general neurology in Forest Hills, New York. In addition to treating a wide variety of general neurology patients in the office and hospital settings, I have treated numerous head injured patients, including athletes of all ages and skill levels as well as non athletes.

In 1994 I was invited by then NFL Commissioner Tagliabue to become an original member of a newly formed scientific NFL committee on mild traumatic brain injury. The goals of that committee were congruent with my goals: to advance the medical/scientific knowledge of concussions and thereby improve the health and safety of NFL players. I joined the committee in an advisory/consultant capacity. I never was an employee of the NFL and I have always maintained my fulltime private practice of neurology. During my fifteen years as a committee member, including three years as co-chairman, we did research on the biomechanics of NFL concussion, the clinical and epidemiologic features of NFL concussion, neuropsychological testing in NFL players and scientific testing of protective headgear. In collaboration with Dr. Albert King of Wayne State University, we studied finite element modeling of NFL concussions. In collaboration with researchers in Sweden, we developed an animal model of NFL concussion.

All of the committee's research and scientific endeavors were conducted in a completely open and transparent fashion. We published our studies in the peer-reviewed medical literature. We participated in vigorous scientific debates.

We invited outside experts from various scientific/medical disciplines, from academia as well as private industry, to attend and speak at our meetings. We have encouraged scientists to study and present their results to the scientific community. The committee has sponsored educational symposia for NFL medical and training personnel to update them on the latest scientific/ medical advances regarding concussion. We invited outside experts to speak at these events. We have shared our findings with Department of Defense medical experts. Although there is always more scientific work to be done, the work of our committee definitely advanced the scientific/medical knowledge of concussions and thereby improved the health and safety of NFL players.

I have been concerned about the possibility of long term effects on the brain related to football for close to thirty years. My studies and investigations on the chronic effects of boxing on the brain have provoked questions and concern regarding the possibility of similar effects related to other contact sports including football. One of the reasons that I was asked to be on the NFL MTBI committee was because of my knowledge of and experience treating boxers with chronic traumatic encephalopathy (CTE).

In 2003, members of our committee began to formulate a plan to scientifically investigate the possibility that there were long term effects on the brain due to a career in professional football. We planned a clinical research study modeled after the study that I had directed on retired boxers in the 1980s. We wanted to undertake a study that would be more exhaustive and include a control group. In order to assure the highest possible scientific quality, we consulted with leading experts from various medical/scientific fields at leading research academic centers around the country. We consulted with neuroradiologic MRI experts at USC, the University of Wisconsin, Mt. Sinai Hospital Medical Center in New York and Dr. Mark Haacke of Wayne State University. We consulted with neuropsychology experts including the president of the National Academy of Neuropsychology and experts at Columbia University in New York and the University of Texas-Southwestern. We consulted experts on APOE genotyping at Duke University. Committee member Dr. Joel Morgenlander, professor of neurology at Duke University, and I formulated a detailed plan for performing comprehensive clinical neurological evaluations. The result

of these efforts was a comprehensive research study employing clinical neurological examinations, comprehensive neuropsychological testing, state of the art MRI imaging of the brain and APOE genotyping to evaluate a large group of retired NFL players and control subjects. The control group consists of age similar men who played college football and then attended NFL training camp but played less than one full regular season in the NFL. The MRI brain protocols and analyses for the study are under the direct supervision of Dr. Mark Haacke of Wayne State University. The statistical analyses used in the development of this study were performed at Wayne State University. The NFL is funding this study.

Despite what inaccurate and distorted media reports have suggested, I have never prejudged the results of this or any other scientific study. I have no bias regarding the outcome of this study. All the examinations and testing for the study (including the neurological examinations) are performed in a completely blinded fashion (the status of the subject as a retired player or as a control is not known to the examiner). All data analyses are performed in a blinded fashion by experts who played no role in the data collection. Since all of the testing is standardized, the data from the retired players can be compared to both the control group and the general population.

The MTBI committee and I have closely followed the medical literature and the reports of studies suggesting a link between professional football and long term brain damage. Based upon three survey type studies in retired NFL players and a small number of case reports of neuro-pathological abnormalities in the brains of retired NFL players, some have suggested that chronic brain damage in football players is an epidemic that constitutes a national health crisis. It is my opinion that there is as yet not enough scientific evidence to support such statements. Clearly there is abnormal tau pathology in the brains of a small number of deceased former NFL players. Some living retired NFL players have experienced neurological/behavioral/psychological problems that may be related to this type of pathology or perhaps to other factors. This is a matter of great concern to me. However, as scientists and physicians it behooves us to carefully analyze the evidence before reaching definitive conclusions.

Three survey studies have been cited as proof that a career in the National Football League increases the risk of dementia and/or depression later in life. All were mail-in surveys or telephone surveys. There are a number of methodological limitations inherent to these types of studies. The data collected is highly dependent on the subjects' motivation and memory. The researchers can never be sure that the percentage of subjects who respond are truly representative of the entire study population. These types of self report questionnaires are limited by response bias (the subjects respond to all the questions in a pattern manner) and social desirability response set bias (subjects' responses are based on what they think they should answer rather than what they may actually think).

These and other problems are readily apparent upon scientific analysis of the two papers from the University of North Carolina regarding the risks of depression and late life cognitive impairments in retired NFL players. It must be pointed out that both of these papers are based upon the same collection of data from the same self report questionnaires mailed to the same subjects and their spouses. In other words, the two papers are the result of one study, not two separate independent studies. The first questionnaire was mailed to 3,683 subjects, of whom 1131 (30.7%) did not respond. A follow up memory questionnaire was then sent to 1,754 retirees over age 50 who had responded to the initial questionnaire; 996 (66.8%) did not respond. There is no way to know if the large numbers of subjects who did not respond would have answered the questions posed in the same way as though who did respond. If many of the non-responding subjects did not answer because they were healthy and had no medical/neurologic or psychiatric complaints, this clearly would have biased the study results toward reporting a higher incidence of cognitive or depression symptoms than was truly present in the entire study population. These studies relied solely upon the memories of the subjects to collect data on concussion history 20 to 50 years in the past. Yet, the authors then reported that many of these same subjects had cognitive/memory problems. This raises serious doubts about the reliability of the data. The absence of a valid control group makes any comparisons to the general population difficult to interpret. The authors attempted to make a comparison to the United States population incidence of dementia but this comparison is invalid because the general population data were not collected from

self report and spouse report questionnaires as was done in this study.

In the paper regarding depression, the authors reported that 11.1% of the entire group had been diagnosed with clinical depression, which they then state is "generally consistent with" the incidence in the general U.S. population. This suggests that retired NFL players do not have an increased risk of depression. The authors then stratified the data and reported that subjects with a history of no concussions had a 6.5% incidence of depression, those with a history of one or two concussions had a 9.74% incidence of depression and those with 3 or more concussions had a 20.17% incidence of depression. Does this mean that professional football players who sustained two or fewer concussions during their careers are somehow protected from (partially immune) to developing depression later in life compared to other American men who never played professional football? Or are these results evidence of a phenomenon known to clinicians and social researchers as "selective memory"? This occurs when subjects who suffer from an illness (in this case depression) unconsciously seek out a cause for that illness and are thus more likely to "remember" prior concussions. These studies also suffer from the absence of any objective verification of the subjects reports. There are no reports of any physical examination findings or diagnostic study findings on any of the subjects.

The third self report "study" recently cited as indicating that retired NFL players have an increased incidence of cognitive/ memory impairments was done at the University of Michigan by Dr. David Weir and funded by an arm of the National Football League. This study has the same limitations and problems as the other two studies, as Dr. Weir himself has clearly noted. One need only review Dr. Weir's testimony to this congressional committee in October 2009 and read his written statement to the NFL MTBI committee in November 2009 to realize that this study did not find evidence that retired NFL players have an increased incidence of cognitive/memory problems. Dr. Weir testified to Congress:" The study was not designed to diagnose or assess dementia. The study did not conclude that football causes dementia." Dr. Weir wrote to the NFL MTBI committee: "The 19:1 ratio reported in The New York Times is just unsupportable given the evidence that the source for the "one" is much too low where we can compare

with true rates. I told that to (New York Times reporter) Schwarz but he chose to ignore it. Again, nothing in this study says there is not a connection between football on any level and subsequent cognitive problems and nothing says there is. The study is mute on this issue but unfortunately the press is not".

I have also analyzed the neuropathology reports from doctors Omalu and Mckee regarding abnormal tau deposition in the brains of retired NFL players. When Dr. Omalu published his first case, I along with other NFL MTBI committee members reviewed the report carefully and found a number of scientific issues with it. We engaged Dr. Omalu and his co-authors in an appropriate scientific debate by writing a letter to the editor of the journal in which the report had been published. Our objections were based on two major areas: 1. Dr. Omalu had claimed that the neuro-pathological findings in his case were consistent with those reported in CTE of boxers by Dr. Corsellis in a classic 1972 paper. Based upon my familiarity and knowledge of Dr. Corsellis' paper and the other scientific literature of CTE in boxers, we pointed out the multiple reasons why the Omalu reported findings were <u>not</u> consistent with the Corsellis report, and (2) we pointed out the numerous limitations in the minimal clinical information reported on the retired player in question and that there were no reports of any objective physician evaluations or diagnostic studies regarding the subject. In our letter we indicated there were major weaknesses inherent in reporting only posthumously obtained historical information from the deceased's family. When Dr. Omalu subsequently published a case report on the neuropathology of a second retired player, we again carefully evaluated the report and expressed our scientific opinions regarding the weaknesses of the paper in a letter to the editor of the journal. We pointed out that the reported neuropathology in the second case was different in many ways from that in the first case. We again noted the dearth of contemporaneously obtained objective clinical information about the subject and the sole reliance on posthumously obtained information from the deceased's family. We also pointed out a number of inconsistencies between the limited clinical information that was presented and the summary and conclusions reached by Dr. Omalu.

In June, 2007, at our invitation, Dr. Julian Bailes presented some of Dr. Omalu findings at an NFL conference

on head injuries for all NFL team medical personnel. At the conference Dr. Bailes indicated that he and Dr. Omalu believed that these neuropathological findings of abnormal tau protein deposition in the brain had caused depression and suicidality in the two retired players whose brains were the subject of the reports in the medical literature and in a few other cases which had not been reported in the medical literature. At the meeting, I disagreed with Dr. Bailes' conclusions and he and I engaged in a scientific debate over this issue. At the end of the meeting, we agreed that more studies and evaluations were needed.

Over the next few months, the MTBI committee and I sought out expert opinions from the most distinguished tau researchers from renowned academic medical centers around the country. These experts indicated to us that no scientific conclusions could be reached from the two case reports and agreed that further studies were necessary. One of these experts, Dr. Peter Davies of the Albert Einstein College of Medicine in New York, became an unofficial adviser to the NFL MTBI committee and has since shared his expertise on tau, CTE, and dementia with us on a regular basis. At one point, Dr. Davies traveled to West Virginia to review some of Dr. Omalu's materials and was given some of the material to study in his own laboratory. Dr. Davies agreed with Dr. Omalu that there is excessive tau pathology but discovered that the tau pathology differed between the cases. Dr. Davies disagreed with Dr. Omalu's conclusions that this pathology is the same as that reported by Dr. Corsellis and that the cause of this pathology is definitely multiple prior head injuries. Dr. Davies raised the possibility that the use of performance enhancing drugs such as anabolic steroids may have played a role in the development of tau deposits in the brain. Dr. Davies is currently studying this issue in his own laboratory.

Early in 2009, Dr. McKee reported a case of excessive tau deposition in the brain of a retired NFL player. She has since reported one such case in the medical literature and a number of others to the media. The NFL MTBI committee and I were immediately very concerned about the implications for the health of NFL players. We invited Dr. McKee to present the findings to the committee and she has subsequently done so on two separate occasions. Dr. McKee has shown cases of abnormal tau deposition in some retired NFL players, some men who had played college football but

never played in NFL and an 18 year high school football player. Dr. McKee has stated to us that these findings can only be due to prior history of multiple head injuries. Despite the absence of any objective of any clinical data obtained on any of the subjects while they were alive, she has stated that posthumously obtained reports from families of the deceased demonstrate that many of these retired players suffer from depression and/or dementia and some suffered from drug abuse, all of which she believes were caused by this tau pathology. Based upon my frequent discussions with Dr. Davies, my own experience with the CTE of boxers, my clinical neurologic experience with concussions in athletes and with clinical neurologic diseases in non athletes, I have carefully analyzed Dr. McKee's reports. I certainly agree that some retired NFL players have abnormal tau pathology in their brains. However the cause of this pathology is still uncertain. Head trauma may be playing a role, but even if it is, we do not know if the significant head trauma occurs in childhood, adolescence or at a later time in life. The presence of tau pathology in the brain of an 18 year old high school athlete and some middle aged men who had played high school and college football but never played in NFL certainly suggest that head trauma in adolescence may be an important factor.

There are a number of other neurologic diseases unrelated to head trauma which are characterized by excessive tau deposition in the brain. These include the frontotemporal dementias, the cause of which is most likely genetic, as well as progressive supranuclear palsy and cortical-basal degeneration, the causes of which are unknown although many researchers suspect some environmental or toxic etiology. The Chamorro Indians of Guam suffer from a disease called the Parkinson's dementia complex of Guam in which excessive brain deposition of tau is very similar to that seen in the football cases and the CTE of boxers. Extensive studies of this disease have not uncovered any genetic component or any relationship to head trauma. Some researchers believe that this Guam disease arises from a toxin in one of the native foods but others dispute this. These diseases remind us that excessive tau deposition can be caused by genetic, environmental or toxic factors in the absence of any history of head trauma. The possibility that the use of performance enhancing drugs such as anabolic steroids, growth hormone or toxic contaminants in these or other substances certainly needs

to be considered in the football cases. It is important to also remember that some tau deposition can also be seen in normal aging brains.

The clinical features of these other tau diseases are much different from those reported in the football cases. Many of the patients with the other tau diseases have clinical features similar to Parkinson's disease. Many boxers with CTE have Parkinsonian features. Yet, none of the football cases have been documented to have any Parkinsonian features during life. Many patients with the other tau diseases including the CTE of boxers had dementia documented and diagnosed in life. Yet, there is no documented objective evidence of dementia in any of the football cases. Although certain behavioral problems have been a part of the clinical picture in some patients with these other tau diseases including the CTE of boxers, depression, suicidality, and drug abuse are not part of this picture. It is difficult to reconcile these facts with the claims that the tau disease of football players is a definite cause of such symptoms in the reported cases.

Depression is well known to have multiple causative factors. Heredity, early childhood life experiences, life stresses such as divorce, financial problems or chronic pain all are important etiologic factors. There is no reason to believe that retired football players are immune from these other possible causes of depression. Dementia is also known to be linked to heredity, cognitive abilities in young adulthood, vascular risk factors such as hypertension, diabetes and heart disease, midlife obesity, alcohol/drug abuse and possibly a prior history of major head trauma. There is no reason to believe that retired football players are immune from these risk factors.

The conclusion that I have reached as a result of these analyses is that there is at present not enough valid, reliable or objective scientific evidence to prove that head impacts from professional football are the cause of chronic brain damage. Association does not prove causation.

Some have suggested that scientific evidence regarding the question at hand is conclusive and that there is no need for further research. I strongly disagree with that position. In the present state, we have a tau pathology condition that can only be diagnosed after death. When treatments that are being currently developed aimed at

eliminating, preventing or inhibiting the deposition of tau in the brain become available, how will any of us know which if any football players might benefit from these treatments while they are alive if we have no way of making the diagnosis before autopsy? We need further scientific research to discover in vivo means of diagnosing tau build-up in the brain. In the present state, many assume that all football players with symptoms of depression or dementia have these as a result of tau pathology. This ignores all of the other conditions and diseases that are associated with dementia and/or depression in the general population. Such thinking does retired players a disservice by not considering the possibility that their symptoms may be related to treatable or otherwise manageable conditions rather than a condition which will inexorably lead to deterioration.

At present, many assume that head injury is the only possible cause of this tau pathology condition. If we ignore the possibilities that genetic, environmental or toxic factors (e.g. the use of performance enhancing drugs) may play a role in the development of this tau condition, we may overlook strategies that ultimately could prevent its occurrence.

I have had the honor and privilege of being a member of the NFL MTBI Committee that advanced scientific knowledge of concussions and thereby improved the health and safety of NFL players. I have been a coauthor of a number of scientific articles that have been published in the peer reviewed medical literature and that have withstood the test of time. I believe that the best way to continue to improve the health and safety of NFL players is through continued scientific research.

Recommendations:

(1) Develop in vivo methods to measure tau in the brain

(2) Continue in depth clinical examinations of retired football players
(3) Conduct in depth clinical psychological and psychiatric examinations of retired football players
(4) Determine the accurate incidence of brain dysfunctions in retired football players and the general population

(5) Conduct comprehensive medical and neurological evaluations on all football players who agree to donate their brains for study after death. This will allow reliable clinic-pathological correlations in the future.
(6) Study the long term effects of use of performance enhancing drugs on brain pathology
(7) Continue efforts to prevent concussions by improving safety equipment and making appropriate rule changes.