Eugene Wigner headed the theoretical physics group crowded into Eckart Hall on the University of Chicago campus. His "brain trust" of 20 scientists studied the arrangement, or lattice, of uranium and control materials for achieving a chain reaction and planned the design of nuclear reactors. Among Wigner's group were Gale Young, Kay Way, and Alvin Weinberg, all of whom later moved to Oak Ridge.

Having a chemical engineering background, Wigner also offered advice to Glenn Seaborg and his staff of University of California chemists, who were seeking to separate traces of plutonium from uranium irradiated in cyclotrons. This task was particularly challenging because to that point no one had isolated even a visible speck of plutonium. By September 1942, the team had obtained a few micrograms of plutonium for experimentation, but they needed much more for additional analysis.

In 1942, Compton brought Martin Whitaker, a North Carolinian who chaired New York University's physics department, to Chicago to help Enrico Fermi and Walter Zinn build subcritical uranium and graphite piles. He later put Whitaker in charge of a laboratory under construction in the Argonne forest preserve on Chicago's southwest side. It was here that Compton initially planned to bring the first nuclear pile to critical mass. A strike by construction workers, however, prevented the laboratory's timely completion. As a result, Compton and Fermi decided to build a graphite pile housed in a squash court under the stands of the University of Chicago's stadium.

Leo Szilard and later Norman Hilberry were placed in charge of supplying materials for the pile experiments. They obtained impurity-free graphite from the National Carbon Company in Cleveland, Ohio, and the purest uranium metal available from Frank Spedding's research team at Ames, Iowa.

Under this University of Chicago football stadium, scientists achieved the world's first nuclear chain reaction.