INTRODUCTION
Asymmetric hearing loss (AHL) may be defined as an interaural difference greater than 10 decibels (dB) using the average value of air conduction thresholds in pure-tone audiometry (PTA) for 500, 1000, 2000, and 4000 Hz frequencies [1]. This type of hearing loss can occur between 2 sick ears or between 1 sick ear and another healthy ear. In the latter case, it would be single-sided deafness (SSD), defined as normal hearing in the healthy ear and any degree of hearing loss in the sick ear. The hearing loss may vary from mild to profound and from conductive to sensorineural or mixed. Therefore, the greater the difference between both ears, the greater is the asymmetry. SSD is an extreme case of this pathology.

This type of hearing loss, particularly when the asymmetry is large, brings up 2 significant issues: first, the lesser benefit obtained from bilateral–binaural hearing [2, 3], and second, the choice of the most suitable treatment within the currently available options—bone-conduction implants (BCI), cross routing of offside signal (CROS), hearing aids (HAs), or cochlear implant (CI).

The combination of CI in 1 ear and HA in the other is called "bimodal stimulation." This type of treatment has yielded satisfactory results in cases of profound sensorineural hearing loss (P-SNHL) treated with CI when there is severe sensorineural hearing loss (S-SNHL) in the contralateral ear stimulated with HA [10-17]. Based on this experience, we consider the following hypothesis: the better the hearing in the ear with HA, the greater is the clinical benefit obtained from bimodal stimulation, once hearing in the contralateral ear with CI is restored. Work in this particular area is limited as it is an emerging indication in CI. Positive experiences in the use of CI for SSD have been recently reported [18-11], but there are still very few findings regarding the use of stimulation when the contralateral ear of CI suffers from moderate to severe hearing loss.

This study seeks to prove the bilateral–binaural advantage in a group of patients treated with bimodal stimulation (CI and HA), with different degrees of hearing loss in their best ear.

MATERIALS and METHODS
A retrospective study was performed on the database of patients implanted in a CI center from January 2009 to January 2013. Out of 900 implanted patients, 31 patients with AHL (3.4% of the total) were recruited for this study. They all presented postlingual hearing loss.
ing loss in the implanted ear. The age at implantation ranged from 18 to 76 years. All patients included in the study had carried CI in the ear with P-SNHL for at least 2 years. In total, 3 groups were set up on the basis of the degree of hearing loss in the ear with HA: Group A, comprising 13 patients with moderate sensorineural hearing loss (M-SNHL) (PTA between 41 and 70 dB HL); Group B, comprising 8 patients with type 1 severe S-SNHL (PTA between 71 and 80 dB HL); and Group C, comprising 10 patients with type 2 severe S-SNHL (PTA between 81 and 90 dB HL).


Pure-Tone Audiometry
Thresholds were obtained for air and bone conduction. We started with air conduction, measuring at octave intervals from 125 Hz to 6000 Hz. We started at 20 dB under the hearing level (HL) mode and increased or decreased the intensity by 5 dB at a time, depending on the results. Once the tone threshold was obtained for a specific tone, we moved on to the next octave. The values obtained are expressed as PTA, which is the dB average for the 500, 1000, 2000, and 4000 Hz frequencies.

Speech Audiometry (Disyllabic Word Test)
The test is performed in a soundproof booth, with the patient located at 1 m from each speaker, at a 45° angle. The intensity of stimulation is 65 dB HL. The speech–audiometric materials are presented once on a compact disk recording. The item cannot be repeated. The patient is tested with CI, HA, and bimodal adaptation. The lists for adults include 20 groups of 25 meaningful, phonetically balanced, disyllabic words [12]. Two groups of words are presented in each session. The patients answer correctly when they repeat the same word, without changing any phoneme. The results are presented as a percentage of correct answers.

Each test was performed before the implantation; at 6 months, 12 months, and 24 months after implantation; and on the last follow-up visit or final checkup (FC). This checkup was defined as the last time when the patient came for a checkup with the bimodal adaptation. The tests were performed on the ear with CI, with HA, and with the bimodal adaptation for each patient. The same surgeon performed implantation all patients. All CIs had been activated 1 month post-implantation, and the map and HA programming had been optimized following the National Acoustics Lab, Non Linear, version 1 protocol (National Acoustics Lab; Macquaire Park, Australia) [13, 14]. Ethical clearance was taken for the study from the institutional ethical committee (Ref No: EO 2/11).

Statistical Processing
To analyze data within each group, the Kolmogorov–Smirnov test was used to verify the normal distribution of the variables. If the distribution was normal at the time of the analysis, a T-test was used with the related variables. When the distribution was nonparametric or the distribution was normal but the “n” in the variable was under 10, the Wilcoxon signed-rank test was used.

To analyze data between groups, the T-test for independent variables was used to normally compare distributed variables using the Levene test to verify the equality of the variance. When the result was nonparametric or normally distributed but the “n” in the variable was under 10, the Mann–Whitney U test for independent samples with the exact significance was used.

The level of significance was set at 0.05 for all analyses, and Statistical Package for the Social Sciences v20.0 (IBM SPSS Statistics; New York, USA) was used as statistics software.

RESULTS
Pure-Tone Audiometry

Compared with the initial audiometric values, all patients with AHL included in the study had an average loss of 102.58±13.9 dB in the implanted ear and 72.2±11.9 dB in the ear with HA. Of the 31 patients included, 13 were men (41.9%) and 18 were women (58.1%). The average age at implantation was 50.7±15 years. The average follow-up time was 85.42±33.23 months. The results per group were as follows:

Group A: This included 13 patients (41.9%). The average hearing loss in the implanted ear was 105.48±16.19 dB, while that in the ear with HA was 60.86±6.6 dB. In total, 4 patients were men (30.8%) and 9 were women (69.2%). Their average age at implantation was 52.6±15.3 years. The follow-up time was 67±25.18 months.

Group B: This included 8 patients (25.8%). The average hearing loss in the implanted ear was 104.37±12.92 dB, while that in the ear with HA was 75.59±2.73 dB. In total, 3 patients were men (37.5%) and 5 were women (62.5%). Their average age at implantation was 50.6±12.7 years. The follow-up time was 90.38±30.45 months.

Group C: This included 10 patients (32.3%). The average hearing loss in the implanted ear was 97.37±11.34 dB, while that in the ear with HA was 84.37±2.5 dB. In total, 6 patients were men (60%) and 4 were women (40%). Their average age at implantation was 48.3±19.4 years. The follow-up time was 103±35 months.

Table 1 shows the results obtained with pure-tone audiometry throughout the study. It shows how the hearing thresholds were stable after the sixth month for the implanted ear and the ear with HA; there were no statistically significant differences throughout the follow-up period. This happened again under the bimodal stimulation when thresholds were around 30 dB on average and the values were kept stable in all groups.

Table 2 shows the increase in pure-tone audiometry for each group and compares each modality. It is worth mentioning that bimodal stimulation was significantly better than monaural stimulation with HA in the free field in Group A after 12 months and better, although not statistically significant, than monaural stimulation with CI. In Group B, bimodal stimulation was better than monaural stimulation with CI, although it did not reach statistical significance in most follow-up visits. When comparing bimodality with the ear with HA,
Table 1. PTA results for Groups A, B, and C. Results are measured in dB throughout the follow-up period

<table>
<thead>
<tr>
<th>Time</th>
<th>Ear stimulated with CI</th>
<th>Ear stimulated with HA</th>
<th>Bimodal condition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A (dB)</td>
<td>Group B (dB)</td>
<td>Group C (dB)</td>
</tr>
<tr>
<td>0 months</td>
<td>105.48</td>
<td>104.38</td>
<td>95.37</td>
</tr>
<tr>
<td>6 months</td>
<td>35.57</td>
<td>35.15</td>
<td>31.5</td>
</tr>
<tr>
<td>12 months</td>
<td>34.13</td>
<td>41.09</td>
<td>34</td>
</tr>
<tr>
<td>24 months</td>
<td>32.98</td>
<td>34.84</td>
<td>39.75</td>
</tr>
<tr>
<td>FC</td>
<td>33.26</td>
<td>39.84</td>
<td>38.87</td>
</tr>
</tbody>
</table>

CI: cochlear implant; HA: hearing aid; FC: final checkup; dB: decibels

Table 2. Absolute differences between hearing conditions for pure-tone audiometry for Groups A, B, and C and their statistical significance. Differences are expressed in dB throughout the follow-up period.

<table>
<thead>
<tr>
<th>Time</th>
<th>CI–HA difference (dB)</th>
<th>Statistical significance</th>
<th>CI–Bimodal difference (dB)</th>
<th>Statistical significance</th>
<th>HA–Bimodal difference (dB)</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 months</td>
<td>44.61</td>
<td>0.001</td>
<td>4.95</td>
<td>0.5</td>
<td>8.15</td>
<td>0.68</td>
</tr>
<tr>
<td>6 months</td>
<td>3.19</td>
<td>0.61</td>
<td>4.95</td>
<td>0.026</td>
<td>12.65</td>
<td>0.003</td>
</tr>
<tr>
<td>12 months</td>
<td>7.69</td>
<td>0.03</td>
<td>4.95</td>
<td>0.26</td>
<td>12.65</td>
<td>0.003</td>
</tr>
<tr>
<td>24 months</td>
<td>12.69</td>
<td>0.011</td>
<td>1.92</td>
<td>0.68</td>
<td>14.61</td>
<td>0.002</td>
</tr>
<tr>
<td>FC</td>
<td>11.25</td>
<td>0.013</td>
<td>3.26</td>
<td>0.09</td>
<td>14.51</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Differences between hearing conditions for PTA in Group A

<table>
<thead>
<tr>
<th>Time</th>
<th>CI–HA difference (dB)</th>
<th>Statistical significance</th>
<th>CI–Bimodal difference (dB)</th>
<th>Statistical significance</th>
<th>HA–Bimodal difference (dB)</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 months</td>
<td>28.79</td>
<td>0.012</td>
<td>3.59</td>
<td>0.22</td>
<td>8.75</td>
<td>0.27</td>
</tr>
<tr>
<td>6 months</td>
<td>5.15</td>
<td>0.4</td>
<td>10</td>
<td>0.028</td>
<td>8.53</td>
<td>0.027</td>
</tr>
<tr>
<td>12 months</td>
<td>1.46</td>
<td>0.49</td>
<td>2.34</td>
<td>0.2</td>
<td>5.93</td>
<td>0.14</td>
</tr>
<tr>
<td>24 months</td>
<td>3.59</td>
<td>0.40</td>
<td>3.75</td>
<td>0.6</td>
<td>8.90</td>
<td>0.048</td>
</tr>
<tr>
<td>FC</td>
<td>5.15</td>
<td>0.14</td>
<td>1.87</td>
<td>0.37</td>
<td>16.87</td>
<td>0.011</td>
</tr>
</tbody>
</table>

Differences between hearing conditions for PTA in Group B

<table>
<thead>
<tr>
<th>Time</th>
<th>CI–HA difference (dB)</th>
<th>Statistical significance</th>
<th>CI–Bimodal difference (dB)</th>
<th>Statistical significance</th>
<th>HA–Bimodal difference (dB)</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 months</td>
<td>13</td>
<td>0.019</td>
<td>3.75</td>
<td>0.23</td>
<td>16.41</td>
<td>0.018</td>
</tr>
<tr>
<td>6 months</td>
<td>12.66</td>
<td>0.033</td>
<td>3.75</td>
<td>0.23</td>
<td>13.37</td>
<td>0.012</td>
</tr>
<tr>
<td>12 months</td>
<td>10.16</td>
<td>0.051</td>
<td>3.75</td>
<td>0.23</td>
<td>13.37</td>
<td>0.012</td>
</tr>
<tr>
<td>24 months</td>
<td>5.15</td>
<td>0.37</td>
<td>1.87</td>
<td>0.37</td>
<td>16.87</td>
<td>0.011</td>
</tr>
<tr>
<td>FC</td>
<td>15</td>
<td>0.032</td>
<td>1.87</td>
<td>0.37</td>
<td>16.87</td>
<td>0.011</td>
</tr>
</tbody>
</table>

PTA: pure-tone audiometry; CI: cochlear implant; HA: hearing aid; FC: final checkup; dB: decibels

Table 3 shows the results of disyllabic word recognition at all points in time during the follow-up. In the ear with CI, results were homogeneous and stable after the sixth month. In the ear with HA, a fall in the recognition was observed after 6 months of follow-up. This fall in speech recognition evolved differently in the 3 groups. Group A achieved complete recovery of recognition, while Group B achieved only partial recovery and Group C achieved none.

When performing analysis between groups, there were statistically significant differences between Group A and Groups B and C at time 0. There were no significant differences in the rest of the values. However, in general, the better the residual hearing of the patient in the ear with HA, the better are the audiometric results, even though statistical significance is not reached (Figure 1).

Speech Audiometry

there were significant differences in favor of bimodality, except at 24 months, when the results improved but there was no statistical significance. In Group C, the ear with CI behaved the same as that in the previous 2 groups. Compared with HA, bimodality yielded significantly better results after the sixth month and then followed the same pattern as that in Group B.
Table 4 analyzes the increases reflected in speech audiometry for each group, comparing each modality. Compared with HA, bimodality yielded a statistically significant improvement in all groups from the sixth month onward, except in Group B’s last checkup. The increase ranged from 8.8% to 38.4% and reached statistical significance above 11%. When performing analysis between groups, there were significant differences between Groups A and C at 12 months and on FC. There were also significant differences in the ears with HA between Groups B and C in the last checkup. The reason behind this was that group C recognition levels had not been recovered following CI activation. This had an impact on the benefits obtained with bimodal stimulation, where there were significant differences from 24 months onward between Groups A and C (Figure 2).

Discussion
Cochlear implant has been traditionally indicated for patients with bilateral, severe to profound hearing loss as well as those with poor speech recognition; it has been the treatment of choice to restore hearing in this group of patients. Results shown in this study, based on PTA, indicate that CI implanted in an ear with P-SNHL is an effective, safe measure to provide stable audibility from the first month of activation. This piece of information is extremely important for the group of patients with AHL because an objective of bimodal adaptations is to obtain better sound perception and ensure hearing through one of the ears, in case the contralateral ear may suffer some type of degenerative pathology, as could potentially be the case with bilateral Meniere’s disease [19], autoimmune hearing loss [20], otosclerosis [21], or some labyrinth malformations [22]. The stable PTA results had already been described by other authors [19, 20], and their homogeneity, regardless of the initial HLs, can be explained by several reasons: 1.) They reflect how the peripheral auditory pathway (superior olivary complex, inferior colliculus) is greatly involved in events of sound perception, and other more central factors of greater variability do not have an impact. 2.) The expertise of the implanting center; all subjects had been operated on by surgeons with an expertise in otology, programmed by the same team of audiologists, followed up under a strict follow-up program; in 90.4% of the patients, the same type of CI had been used.
The results of PTA in the ear with HA showed a similar trend to those in the implanted ear. The PTA values were stable throughout the follow-up period, with a mild tendency to worsen as the follow-up period extended. This increase in the tone threshold, despite not being significant in any of the groups, basically depends on an important deterioration of the 4000 Hz frequency, which is compensated by the rest of frequencies when calculating PTA. This occurrence is because of the inner ear’s involution due to old age, compounded with other etiopathogenic factors such as ototoxicity, exposure to noise, proinflammatory agents, and metabolic deregulation [21, 22]. The clinical history and average age of our patients are within this etiopathogenic profile. This underscores the previous point regarding the stability of the results obtained with the CI treatment for AHL to compensate for a potential hearing deterioration of the contralateral ear with better HLs in the initial stages of the evolution.

The same trend was observed with regard to bimodal stimulation. However, there was a difference of approximately 10 dB between the increase obtained after 6 months in Group C and the increase obtained in the last checkup. This was not observed in groups with better residual hearing in the ear with HA. The deterioration of tone thresholds in the ear for Group C is in line with previous remarks and with how the “early” implantation of the ear with P-SNHL in a case of AHL can improve the quality of life of these patients, without having to wait for a severe to profound hearing loss in the contralateral ear. In any case, if this were to happen, this ear would also benefit from sequential, bilateral implantation [23, 24].

In short, with regard to the results obtained with pure-tone audiometry, bimodal stimulation offers better results than monaural stimulation; the difference in each group ranges from 2 to 6 dB, which is in accordance with the values reported in the literature, because the signal is redundant [25] or because of the binaural summation effect of the signal [2, 26, 27]. When analyzing the results between the groups, Group A showed better values in bimodal stimulation than the 2 groups with severe hearing loss (B and C), although there was no statistical significance (Figure 1). Similarly, Group B showed better results than Group C, although there was no statistical significance.

With regard to speech audiometry, the ear with CI showed a progressive improvement in recognition over the 6 months following activation. All groups presented stable results after that point. However, it is worth mentioning that Group C presented an upward trend in disyllabic word recognition during the follow-up, which coincided with the fall in recognition obtained by the ear with HA (Figure 2). The 3 groups showed homogeneous results in disyllabic word recognition at 65 dB with CI, which was expected as all groups initially shared P-SNHL and similar demographics. This result also matches the findings of pure-tone audiometry. The recognition reached by all groups with the implanted ear in cases of AHL is also worth mentioning:

<table>
<thead>
<tr>
<th>Time</th>
<th>CI–HA difference (dB)</th>
<th>CI–Bimodal difference (dB)</th>
<th>HA–Bimodal difference (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 months</td>
<td>49.85</td>
<td>10.82</td>
<td>24.97</td>
</tr>
<tr>
<td>6 months</td>
<td>14.15</td>
<td>0.09</td>
<td>12.54</td>
</tr>
<tr>
<td>12 months</td>
<td>11.38</td>
<td>23.92</td>
<td>11.61</td>
</tr>
<tr>
<td>24 months</td>
<td>4.53</td>
<td>16.15</td>
<td>11.61</td>
</tr>
<tr>
<td>FC</td>
<td>1.46</td>
<td>12.76</td>
<td>15.23</td>
</tr>
</tbody>
</table>

DWR: disyllabic word recognition; CI: cochlear implant; HA: hearing aid; FC: final checkup; dB: decibels

Table 4. Absolute differences between hearing conditions for the disyllabic word recognition for Groups A, B, and C and their statistical significance. Differences are expressed in % of correct disyllabic words throughout the follow-up period. FC stands for final checkup.
is comparable with the recognition observed in a population with bilateral P-SNHL and unilateral implantation [28-30].

A fall in recognition was observed in the ear with HA after 6 months. As described, it evolved differently in the 3 groups. We believe that the reason behind this result is the different configuration of the auditory input received by the central auditory system. In general, the better quality stimulus received by 1 of the 2 ears is prioritized, without prejudice to being able to merge the electrical and acoustic signals coming from both ears at the same time, which determines why these patients normally have better results with bimodal stimulation. Therefore, the results of this study agree with those reported in the literature [25, 31, 32], showing the advantages of binaurality–bimodal stimulation. Besides, the results of this study agree with the experience of implantation in SSD cases, where CI plays a role in enhancing binaural auditory perception [8, 10, 11] and even becomes a great palliative tool in cases of tinnitus [9].

With regard to the main objective of this study, the best results were obtained by Groups A and B (Figure 2), i.e., cases where HLs in the ear with HA were better. Therefore, the auditory asymmetry between both ears does not hinder bimal stimulation but rather encourages better results. Therefore, we are in favor of this emerging indication for implantation in AHL when the contralateral ear presents with moderate to severe type 1 hearing loss. The involvement of auditory neural plasticity mechanisms make electric and acoustic stimulation compatible in the central auditory system, as proven by Kral et al. [33, 34] in experimental studies and Petersen et al. [35] using functional neuro-imaging studies with auditory positron emission tomography (PET).

Bimodal stimulation, both in pure-tone and speech audiometry, yields better results than any monaural hearing modality, regardless of whether HA or CI is used.

The auditory asymmetry between both ears is not a barrier for bimodal stimulation but rather favors better results. Therefore, we are in favor of this emerging indication for implantation in AHL when the contralateral ear shows moderate to severe type 1 hearing loss. The involvement of auditory neural plasticity mechanisms make electric and acoustic stimulation compatible in the central auditory system, as proven by Kral et al. [33, 34] in experimental studies and Petersen et al. [35] using functional neuro-imaging studies with auditory positron emission tomography (PET).

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of the Health Department of the Government of Navarra.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.


Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES